TCT Asia

Seoul, April 29, 2010

MDT / Core Valve

Device Evolution, Technique and Clinical Trial Update

Eberhard Grube, MD, FACC, FSCAI

Intl. Heart Center Rhein-Ruhr, Essen, Germany

Hospital Oswaldo Cruz - Dante Pazzanese, São Paulo, Brazil

School of Medicine, Stanford University, Palo Alto, USA

Disclosure Statement of Financial Interest

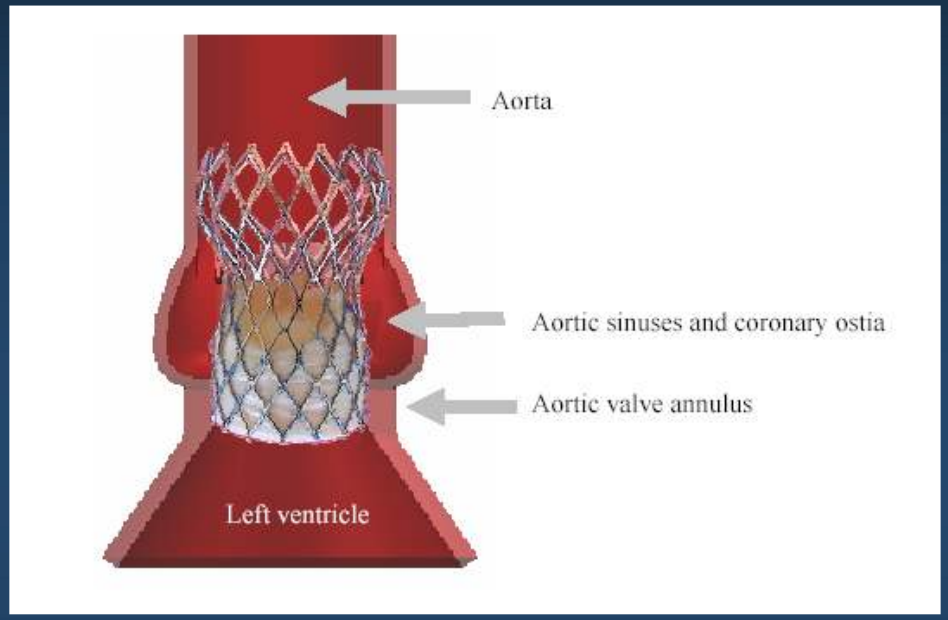
Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

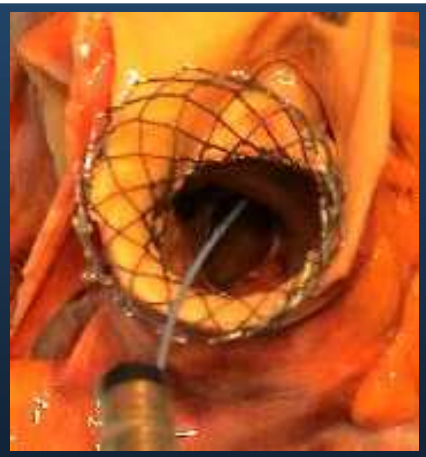
Physician Name	Company/Relationship
Eberhard Grube, MD	**M**edtronic, CoreValve: C, SB, AB, OF Sadra Medical: E, C, SB, AB Direct Flow: C, SB, AB Mitralign: AB, SB, E Boston Scientific: C, SB, AB Biosensors: E, SB, C, AB Cordis: AB Abbott Vascular: AB Capella: SB, C, AB Devax: SB, AB,

Key

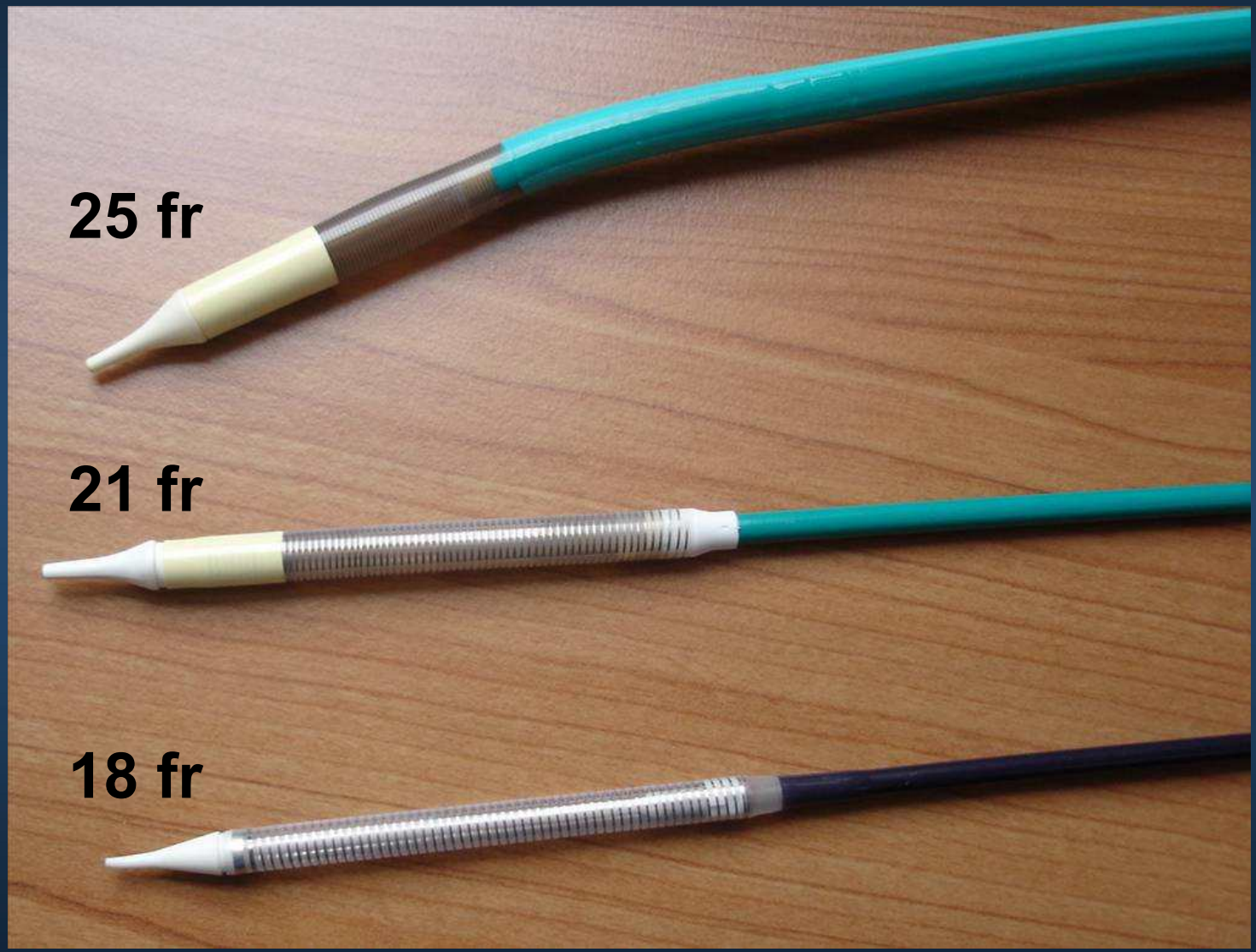
G – Grant and or Research Support
C – Consulting fees, Honoraria
SB – Speaker's Bureau
E – Equity Interests
R – Royalty Income
O – Ownership
S – Salary, AB – Advisory Board
I – Intellectual Property Rights
OF – Other Financial Benefits`

CoreValve Prosthesis





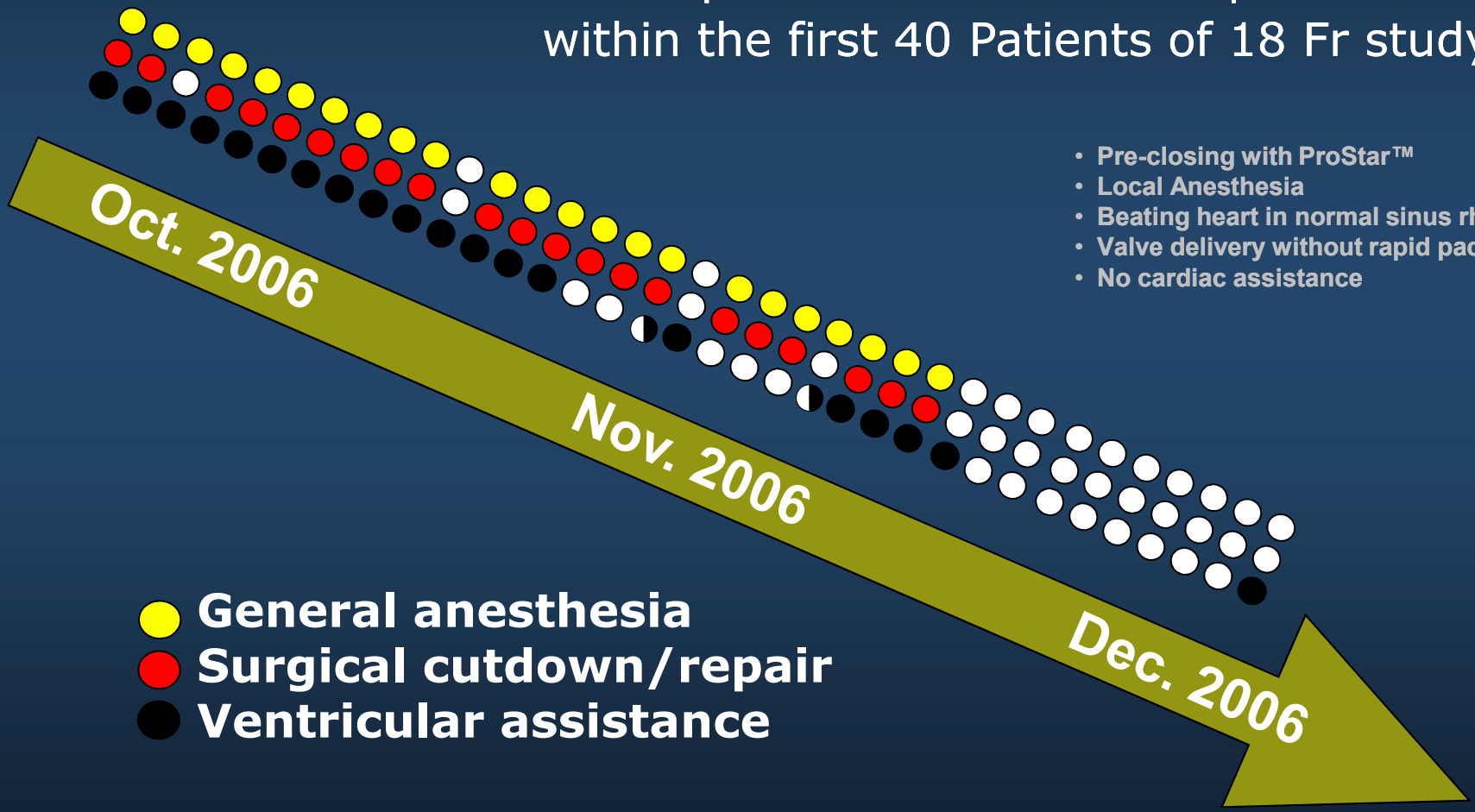
CoreValve : 3 Generations



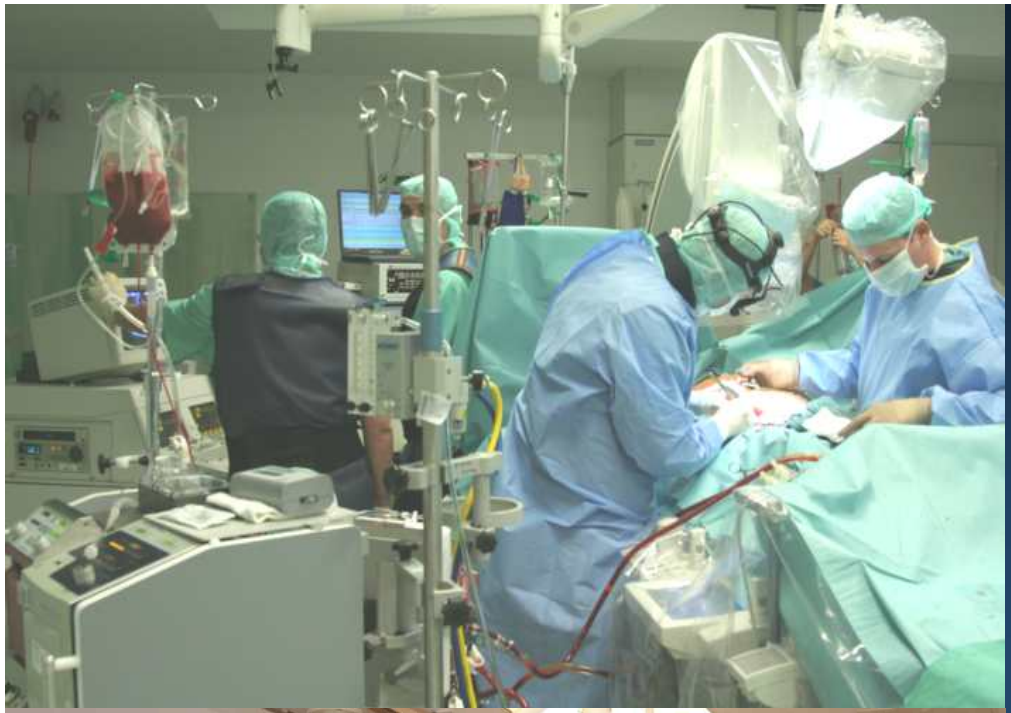
B.Sauren

18 French Procedural Progress

Evolution to a
« true percutaneous cath lab procedure »
within the first 40 Patients of 18 Fr study

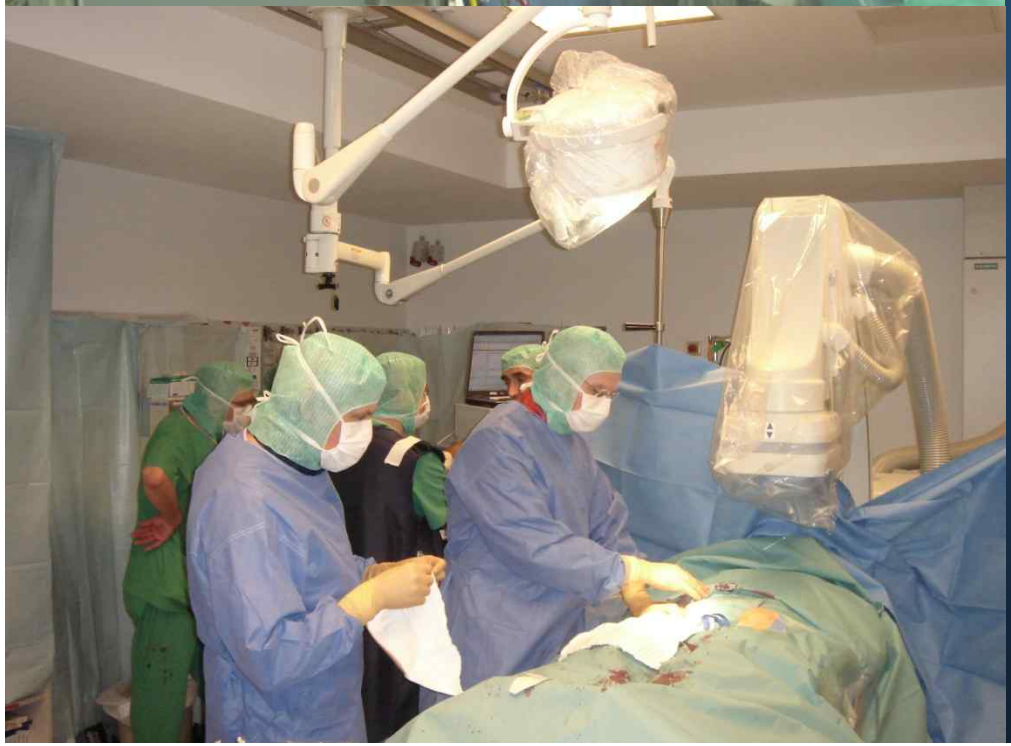


- Pre-closing with ProStar™
- Local Anesthesia
- Beating heart in normal sinus rhythm
- Valve delivery without rapid pacing
- No cardiac assistance



CoreValve 2005

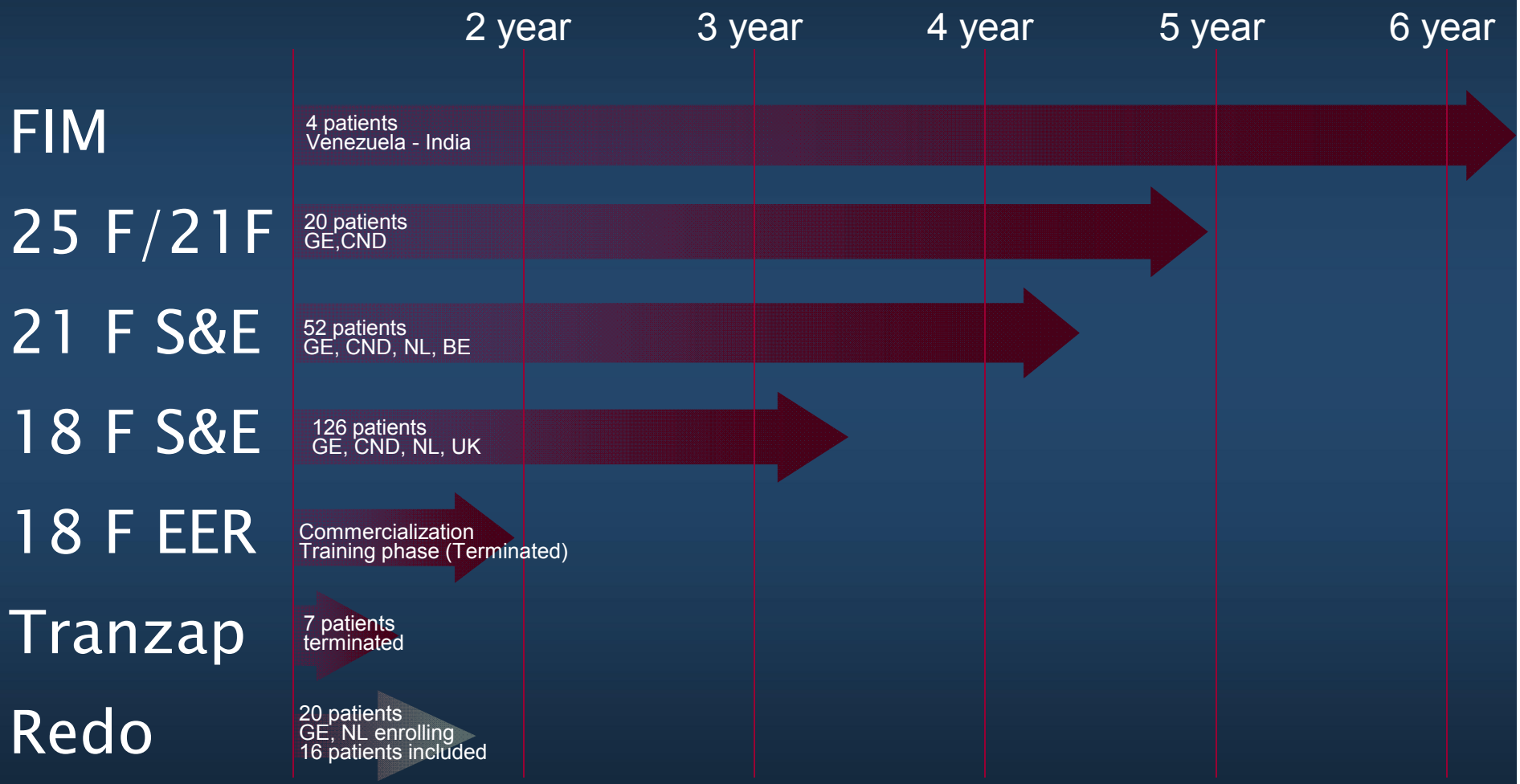
- 24 F 1st Gen CoreValve
- Surgical Prep
- CPB pump
- General anesthesia



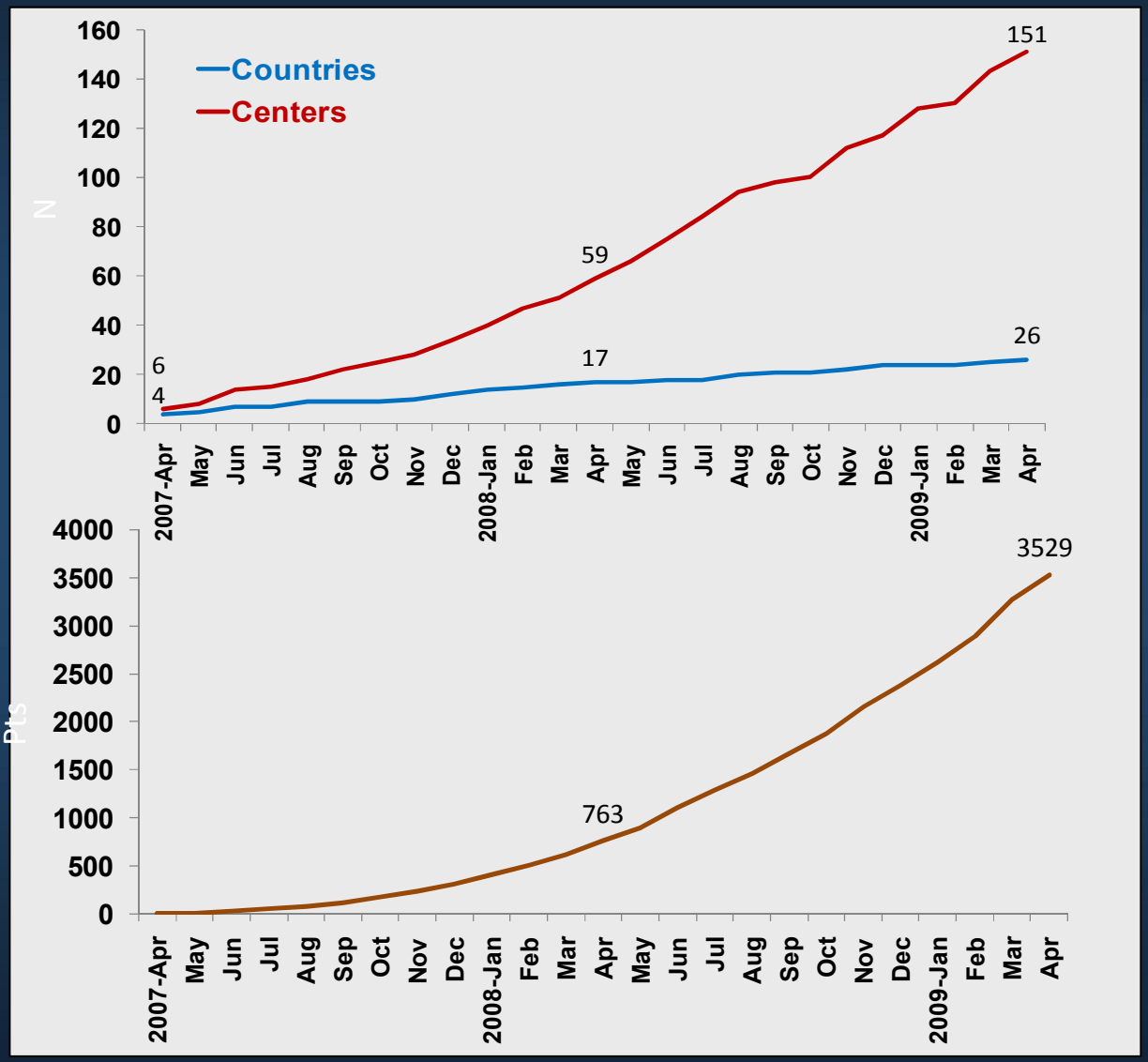
CoreValve 2010

- 18 F 3rd Gen CoreValve
- PCI-like procedure

Corevalve clinical program- FU status



Number of Countries/Centers and Patients



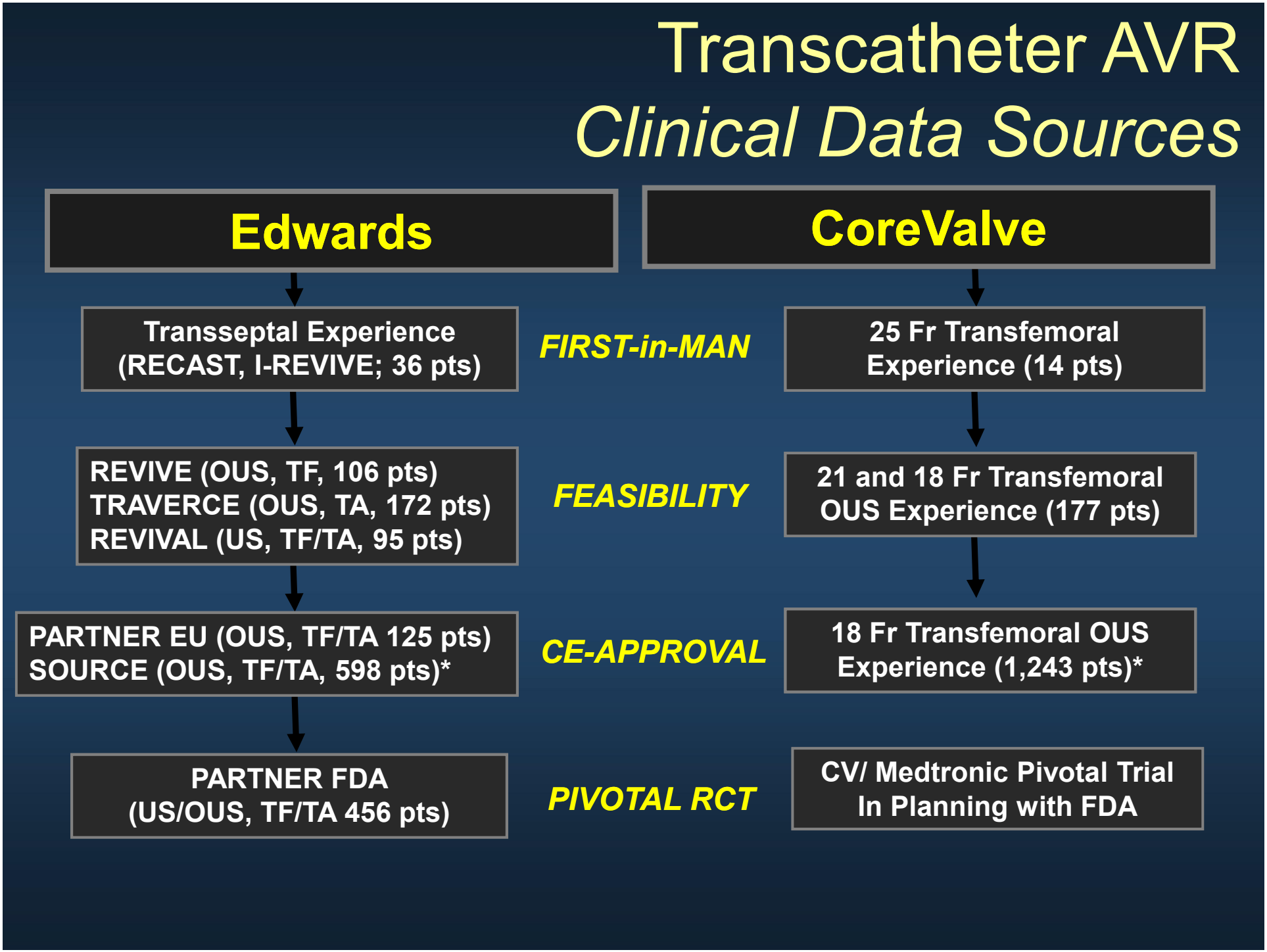
Europe - 20 Countries
- (132 Centers)

South America - 3 Countries
- (11 Centers)

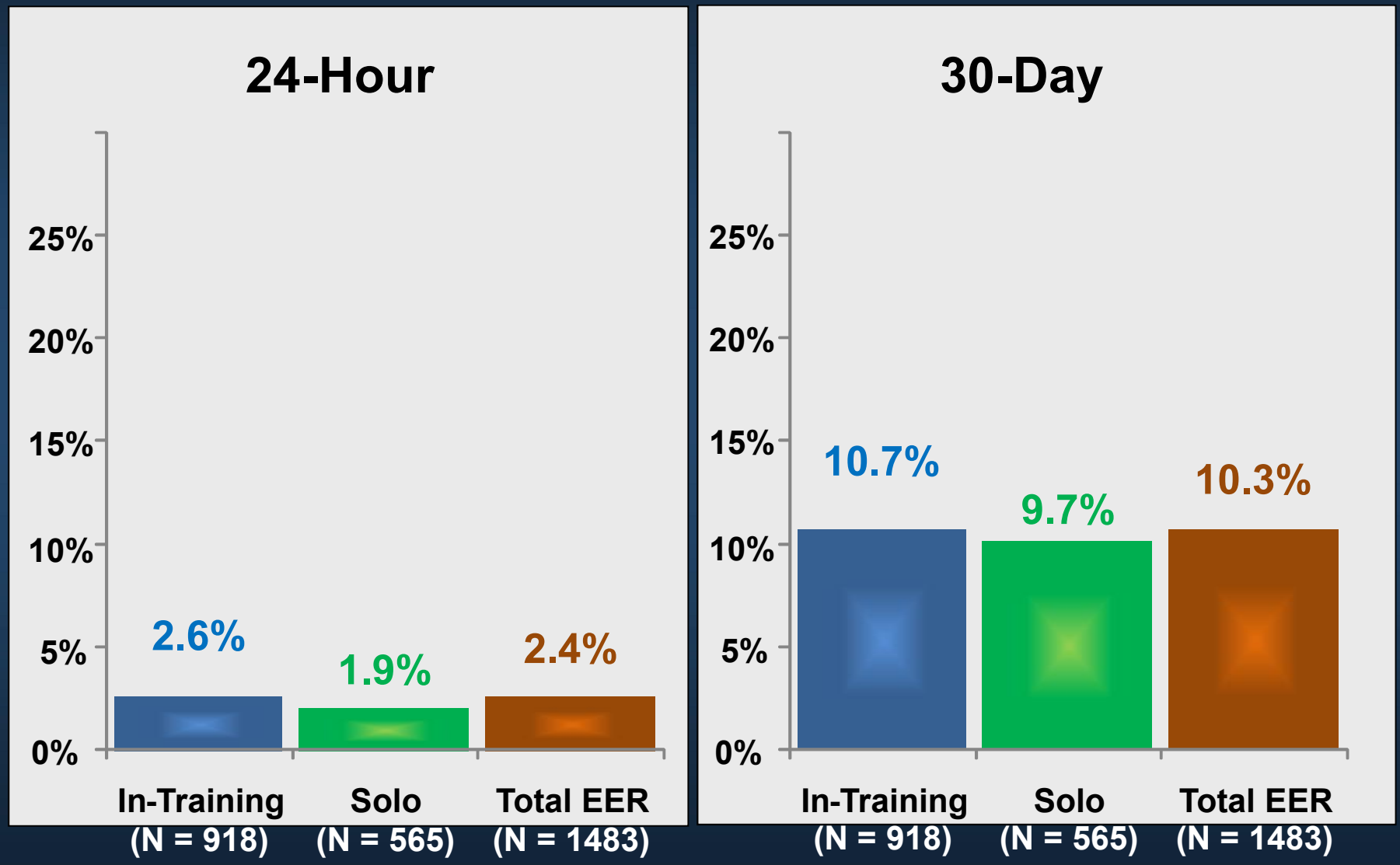
Pacific Rim - 2 Countries
- (6 Centers)

North America - 1 Country
- (2 Centers)

Transcatheter AVR
Clinical Data Sources



CoreValve Mortality Rate



30-Day Adverse Events*
(Site Reported & Non-adjudicated)

	In-Training	Solo	Total EER
Cardiac† Death	6.4%	7.0%	6.7%
Aortic Dissection	1.2%	0.5%	0.9%
Cardiac Perforation	3.0%	2.1%	2.7%
Cardiac Tamponade	4.2%	2.6%	3.6%
Access Site Bleeding	3.5%	1.9%	2.9%
Major Bleeding	8.2%	4.7%	6.9%
Conversion to Surgery	0.5%	1.2%	0.8%
Myocardial Infarction	0.9%	0.9%	0.9%
Major Arrhythmia	16.3%	14.9%	15.7%
Permanent Pacemaker	25.7%	23.9%	25.0%
Renal Failure	2.2%	2.3%	2.2%
Stroke	2.2%	2.3%	2.2%
TIA	0.4%	0.4%	0.4%

Data inclusive of 24-Hour AE and % includes reported AE from cases w/ outstanding 30-day follow-up
*Multiple events in same patients = data not cumulative
†Includes deaths where cause is not known

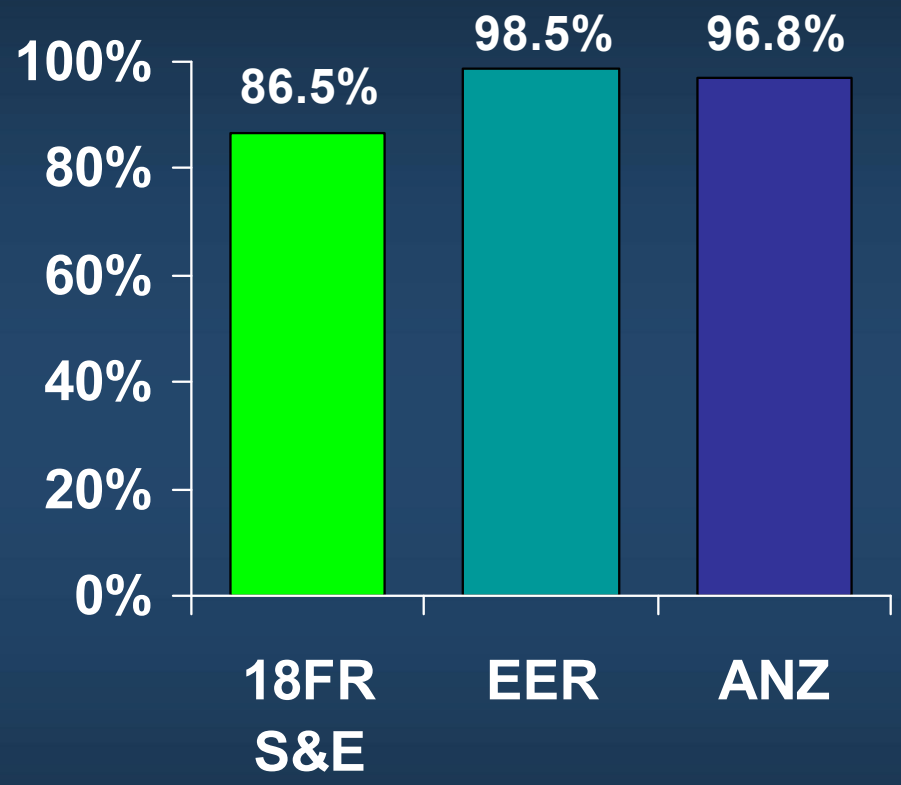
Overall Clinical Experience

Study	N	Follow-ups	Status
18 Fr Safety and Efficacy Trial	126	4 years	On-going
Australia-New Zealand Registry	140	2 years	On-going
Italian Registry	514 to date	6 months	On-going
German Series, Siegburg	>536 to date	30 days	On-going
Expanded Evaluation Registry	1483	Up to 2 years	Completed
French Registry	78 to date	6 months	On-going
Advance Study	1,000	Up to 10 years	Upcoming
US IDE Study	TBD	TBD	Upcoming

Baseline Clinical Characteristics

	18 Fr S&E (N=126)	Siegburg (N=86)	ANZ (N=62)
Age (years)	81.9 ± 6.4	82.3 ± 5.9	83.7 ± 5.4
Female	72 (57.1%)	56 (65%)	30 (48.4%)
NYHA Class I and II **NYHA Class III and IV**	32 (25.4%) 94 (74.6%)	15 (17%) 71 (83%)	11 (19.3%) 46 (80.7%)
Logistic EuroSCORE (%)	23.4 ± 13.8	21.7 ± 12.6	18.7 ± 12.9 (N=58)
Peak Pressure Gradient (mmHg)	72.8 ± 23.0	70.9 ± 22.8	18.7 ± 12.9 (N=58)
Mean Pressure Gradient (mmHg)	47.8 ± 14.3	43.7 ± 15.4	48.6 ± 16.3
Aortic valve area (cm^2)	0.73 ± 0.16	0.60 ± 0.16	0.7 ± 0.2

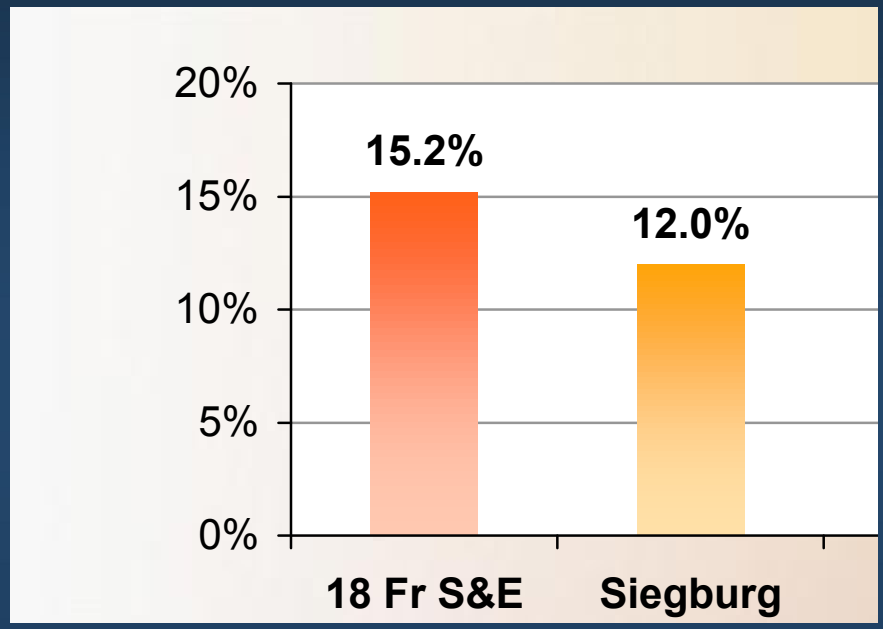
Procedural Success



Procedural success has markedly improved over time

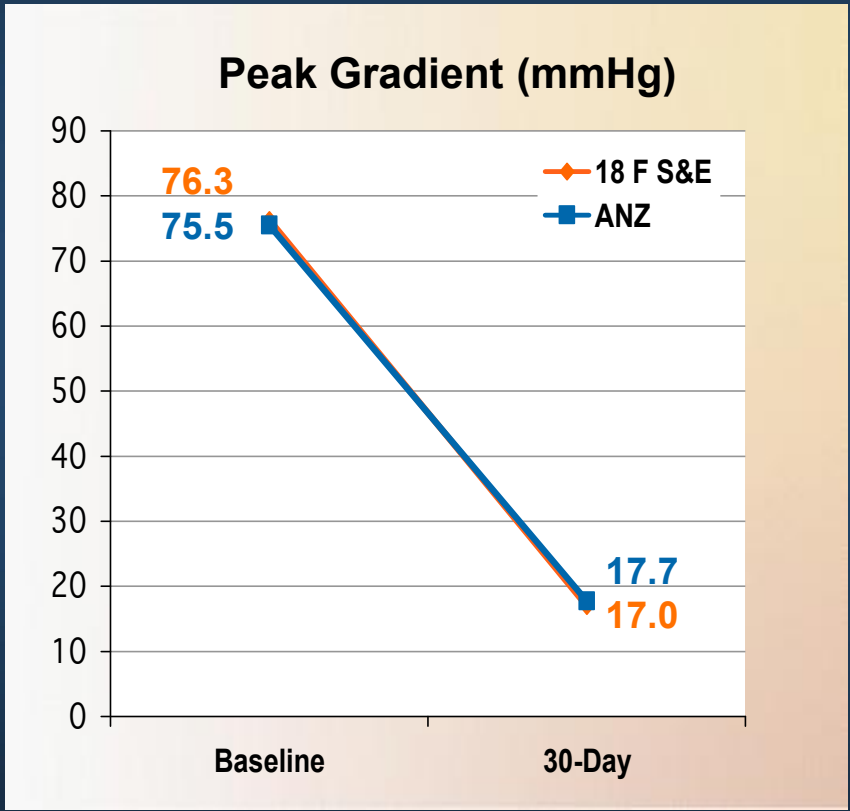
Successful implant defined as no conversion to surgery or device-related mortality during the procedure and proper valve function immediately post-implant. The 18Fr S&E uses technical success (procedural success in re-adjudicated data was 72.6%).

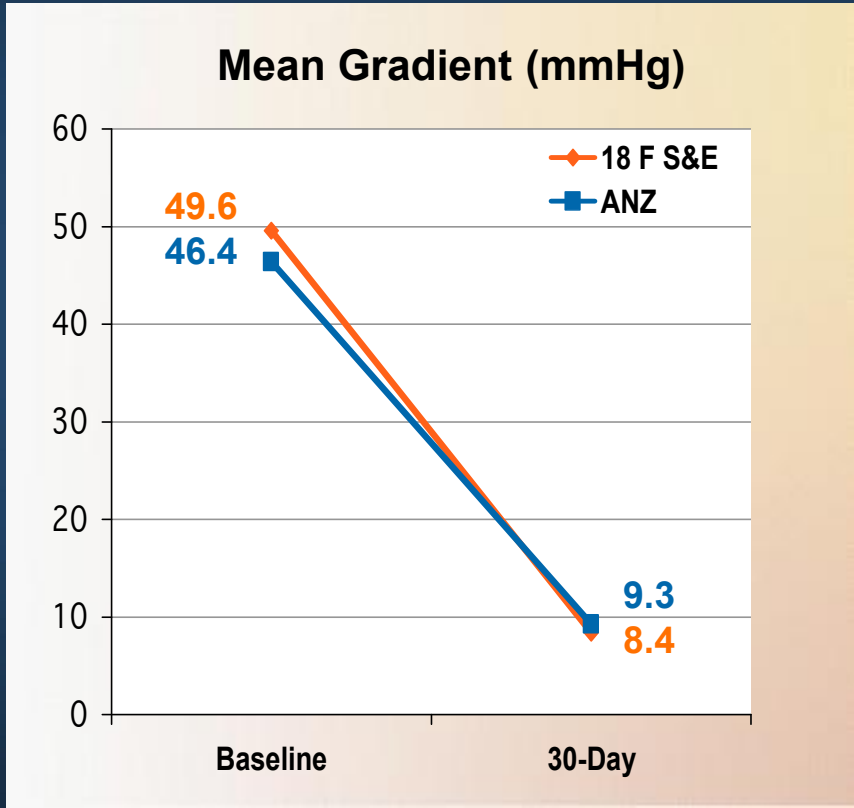
30-Day All-Cause Mortality



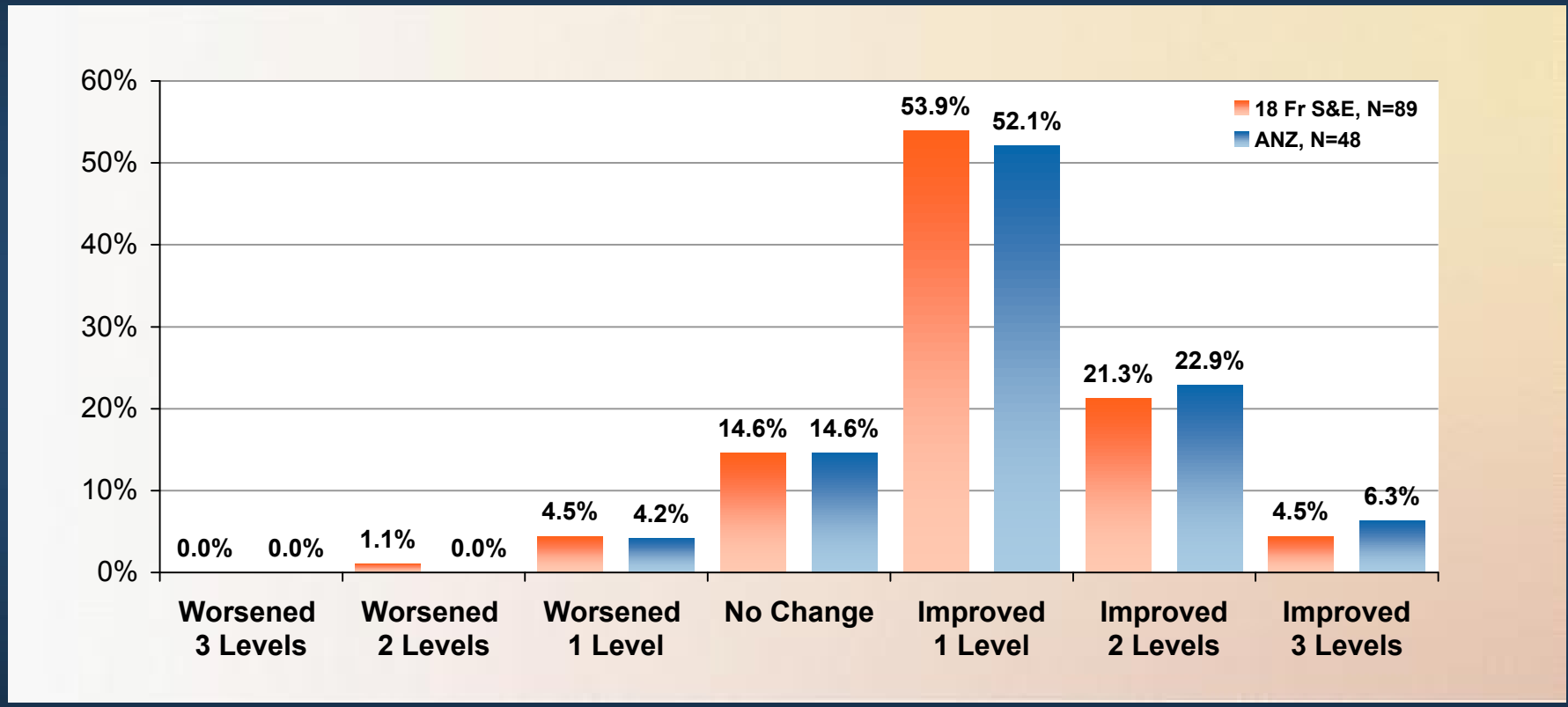
30-day all-cause mortality has improved over time

Pre- and Post-operative Gradients





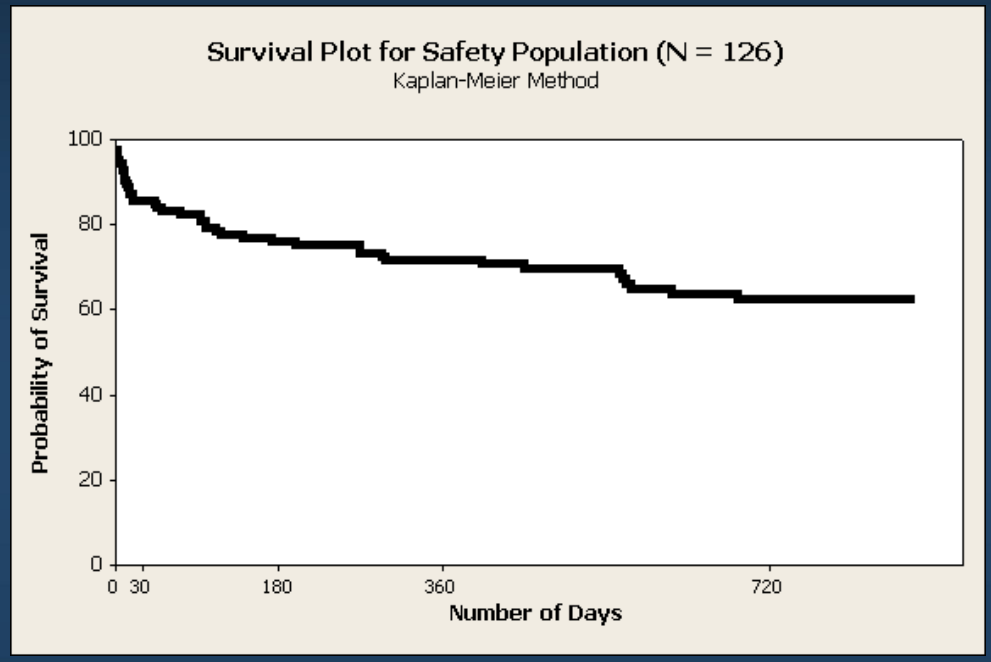
Change in NYHA Class



Paired 30-Day NYHA Classification

CoreValve long term outcomes are quite positive

- In over 7,500 implants, not a single device migration or fracture was ever reported
- The higher leaflets are intended to promote leaflets long term durability and performance
- Two-year follow up of 18 Fr S&E shows 63% survival
- Longest implant to date from 2004; patient still alive and well.



Number at Risk	126	107	93	78	45
Number Failed	3	18	30	35	43
Survival (%)	97.6	85.7	76.0	71.8	62.7

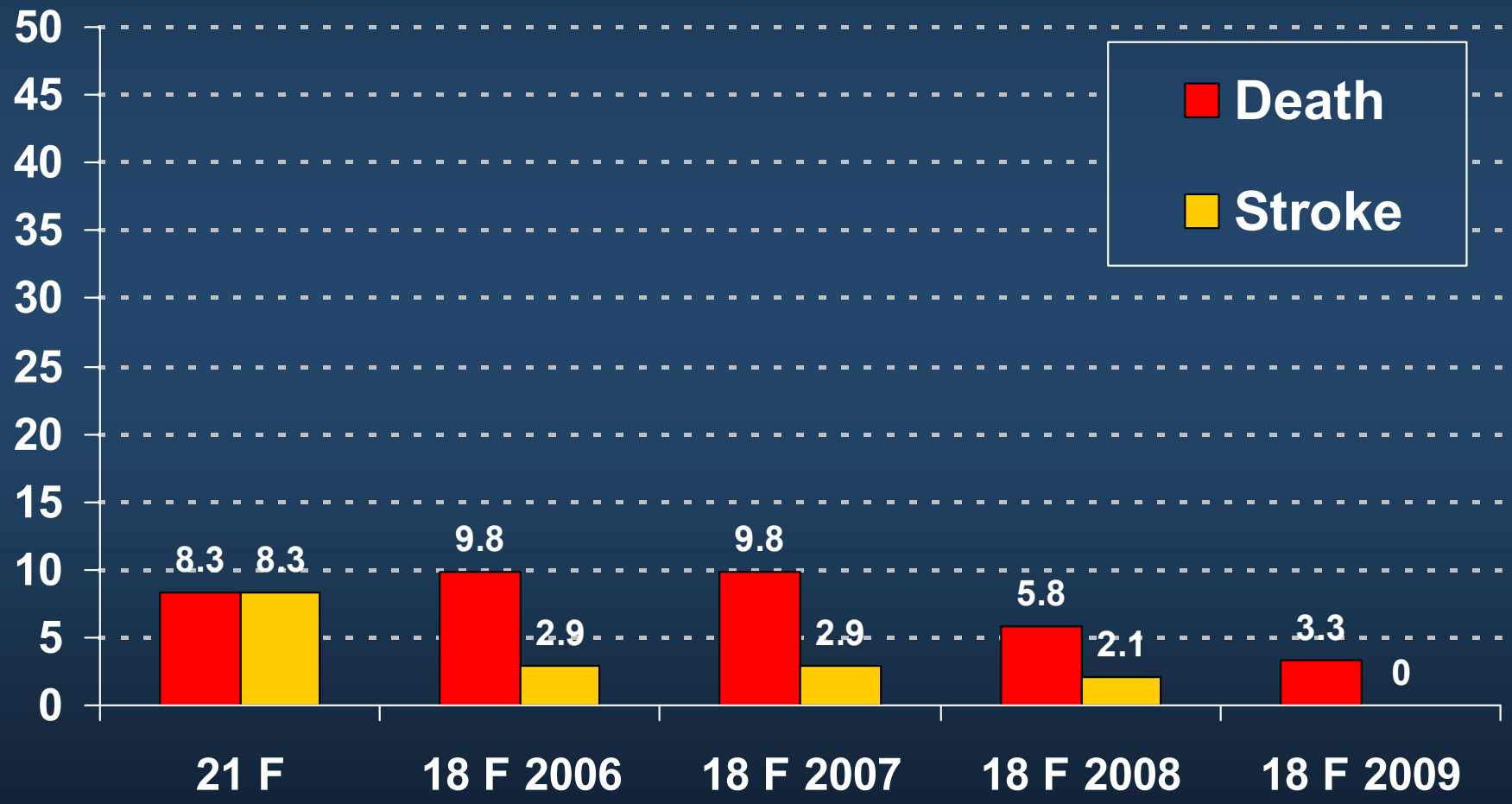
Source: 18 Fr S & E Study: Long-Term Survival

Siegburg CoreValve TAVI Experience

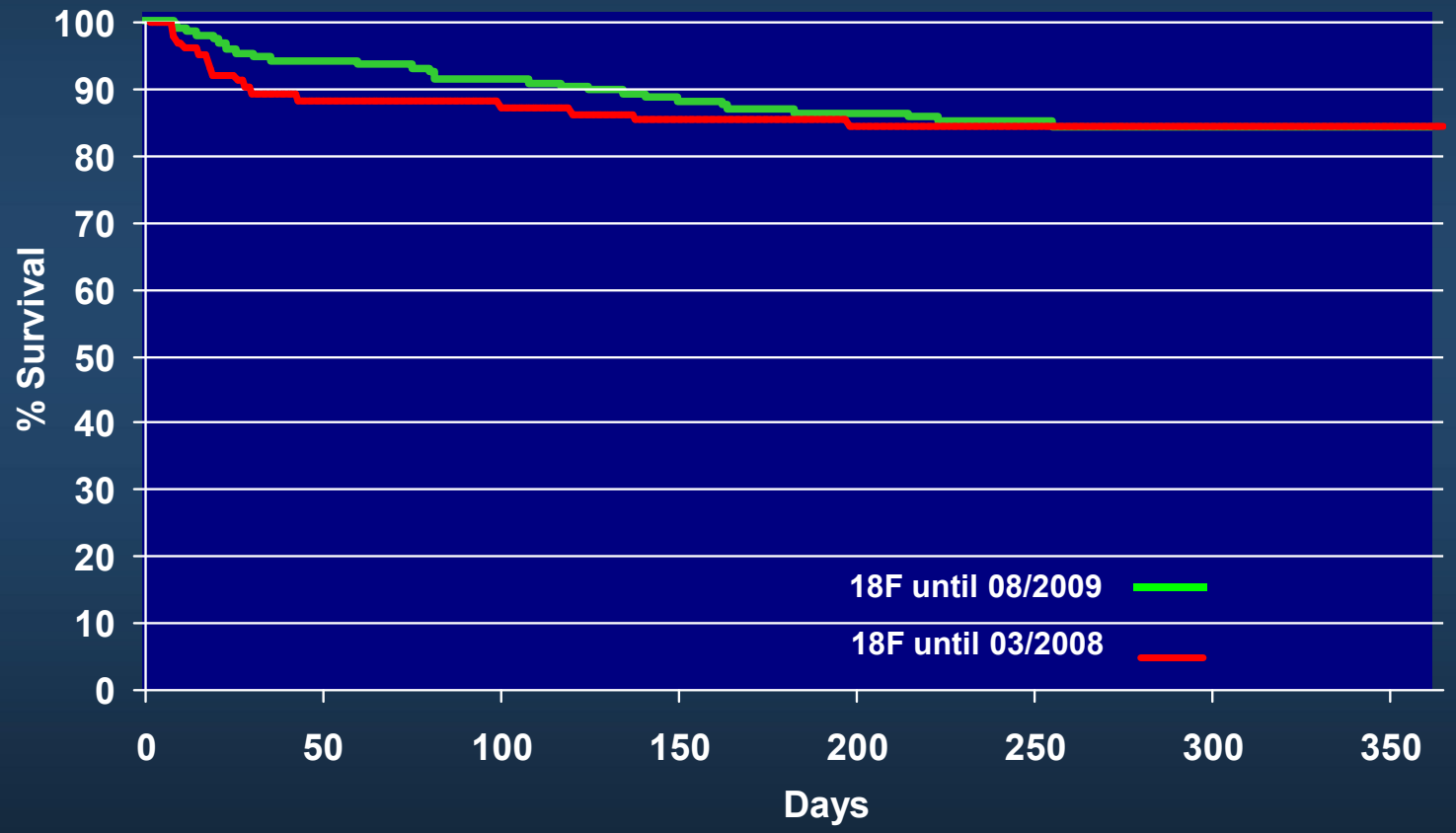
Study	25 F	21 F	18 F S&E	18 F 2008	18 F 2009
Patient n	10	24	102	187	253
Time period	2004 -	2005	03/2006 to 03/2008	01/2008 to 12/2008	01/2009 to 12/2009

Five years, Three generations, 576 patients

In-hospital Events (%)
Siegburg CoreValve TAVI Experience



CoreValve Clinical Results
HELIOS Heart Center Siegburg



Survival Curves up to 1 Year

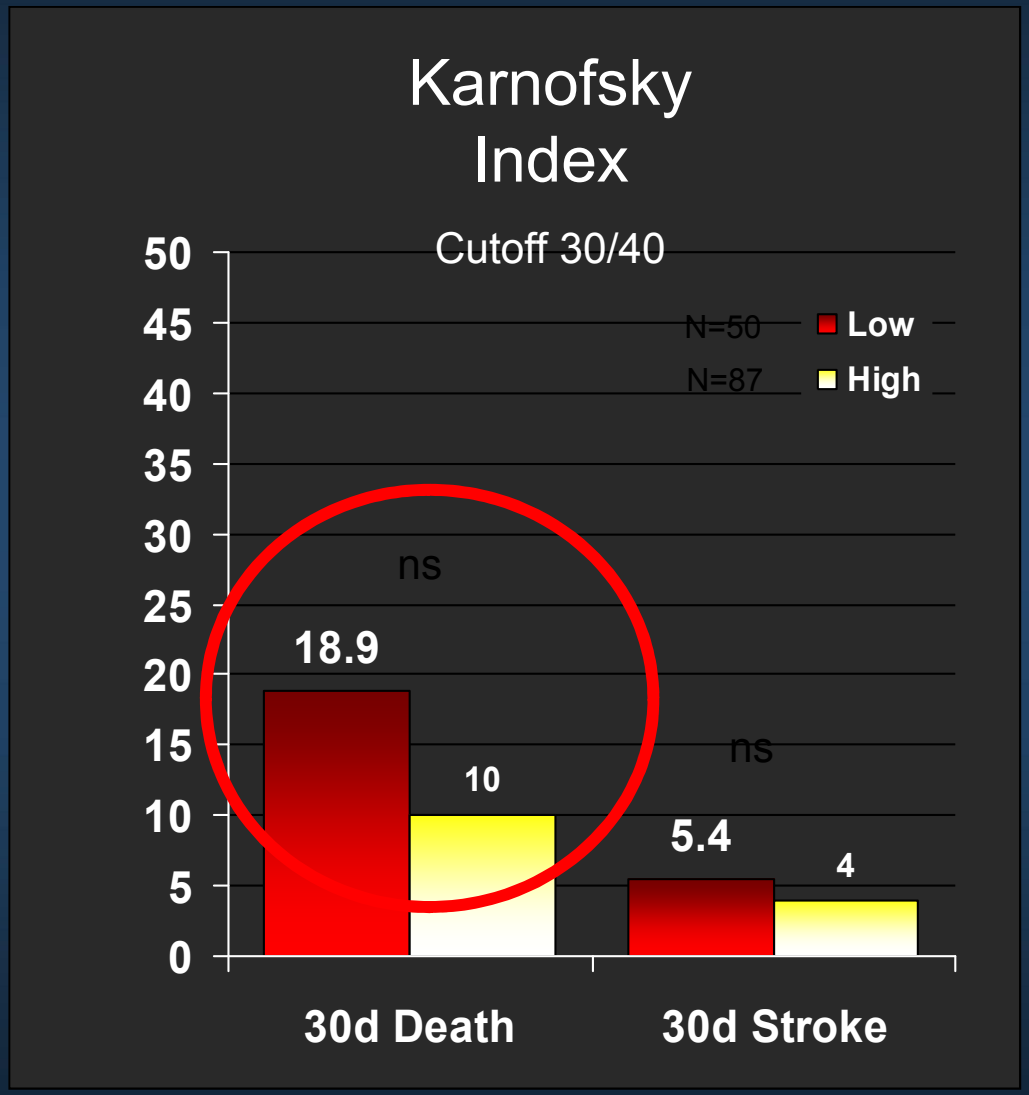
CoreValve Results
HELIOS Heart Center Siegburg

	25F	21F	18F **
Patients, (n)	10	24	102
Age (years±SD)	79.1±4.6	81.7±5.2	81.8±7.4
NYHA class III and IV, n (%)	10 (100)	23 (95.8)	97 (95.1)
Karnofsky index, mean±SD	33.3±7.1	40.7±11.5	44.9±12.4*
Logistic EuroSCORE, %, mean±SD	18.3±5.4	21.1±14.8	24.5±15.4*
STSscore — mortality,%, mean±SD	11.5±10.8	9.1±±.5	8.6±4.7
Left ventricular ejection fraction, %, mean±SD	51.2±15.8	52.8±17.5	51.0±17.3
Peak pressure gradient, mmHg, mean±SD	72.1±27.7	67.9±22.3	71.1±24.6
Mean pressure gradient, mmHg, mean±SD	45.8±20.4	42.2±17.5	41.6±16.4
Aortic valve area, cm2, mean±SD	0.70±0.14	0.74±0.24	0.64±0.18
Annulus diameter, mm	24.1±1.1	23.5±1.5	23.8±1.8
Aortic regurgitation (pre) 3+ and 4+, n (%)	0	1 (4.2)	2 (2.0)

*Significant difference 18F vs pooled 25/21F.**Statistic for the first 102 patient

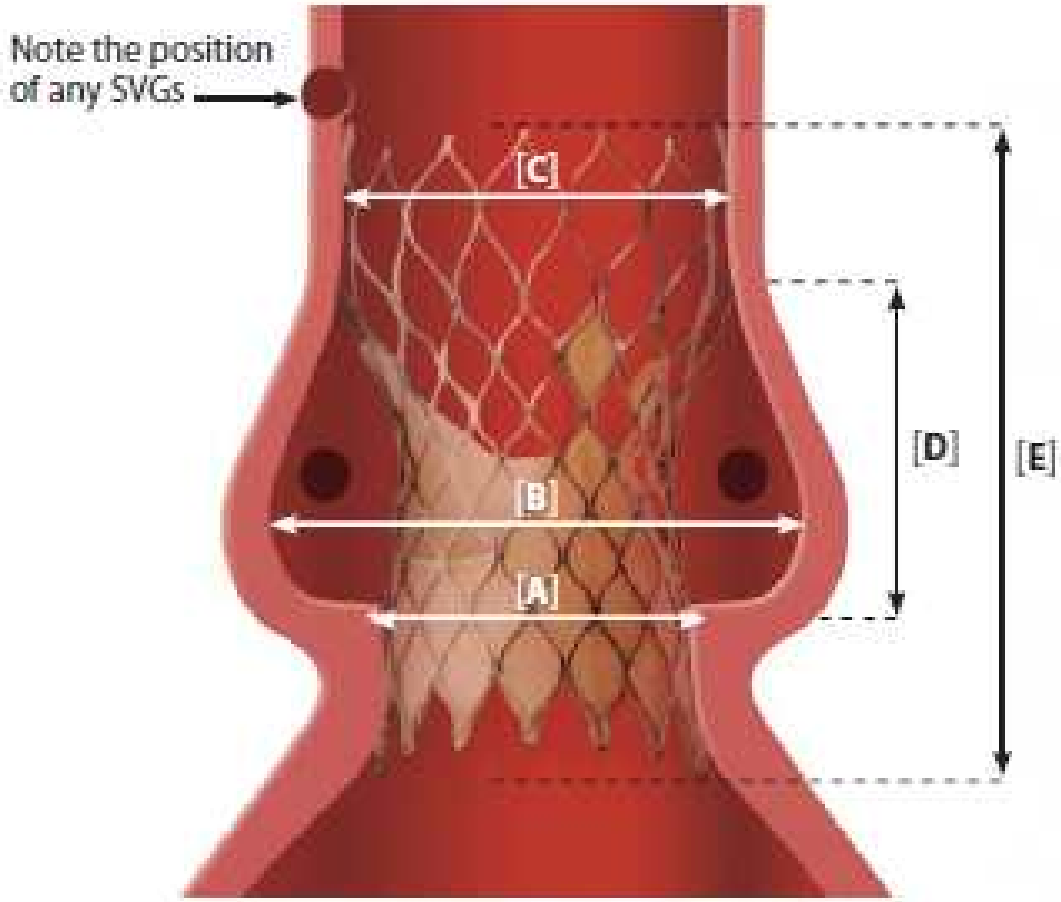
Grube E, Circ Cardiovasc Intervent 2008;1;167-175

CoreValve Results
HELIOS Heart Center Siegburg



Functional status might affect patient outcome

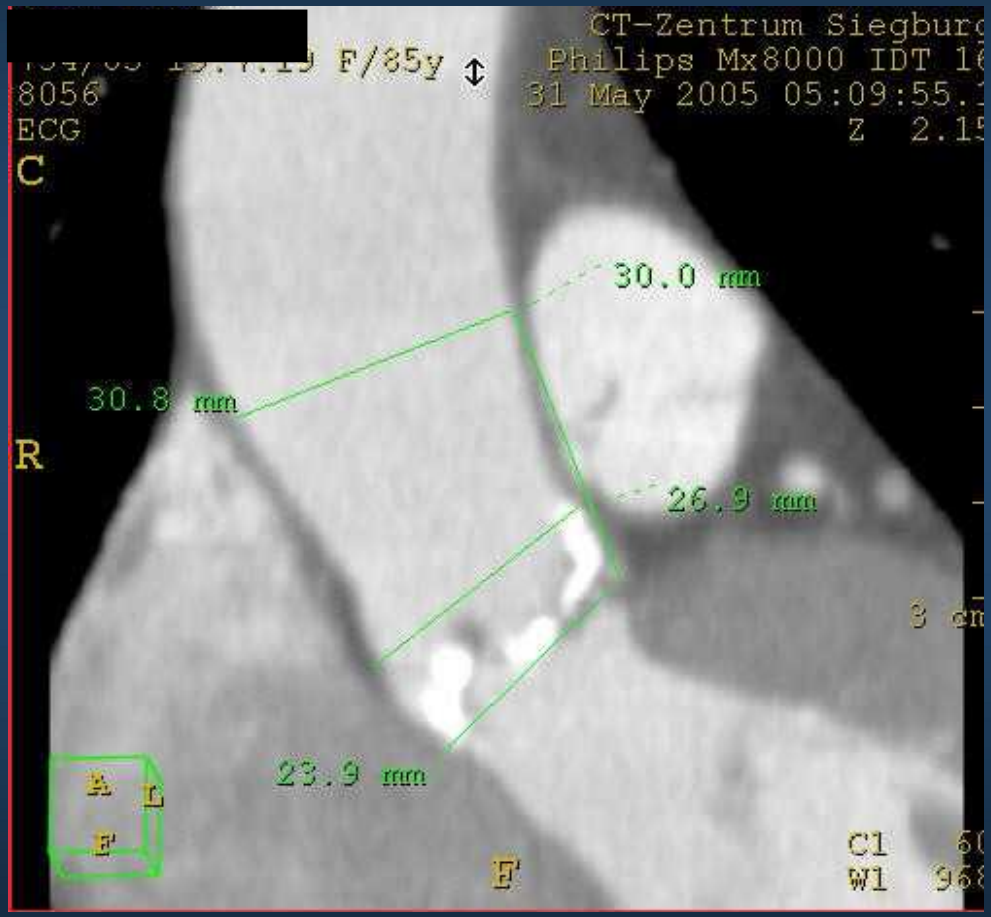
Screening



[A] Annulus Diameter
[B] Sinus of Valsalva Width
[C] Ascending Aorta Diameter
[D] Sinus of Valsalva Height
[E] Frame Height (≈ 5 cm)

illustration not to scale.

CT Screening for Morphologic Quantification



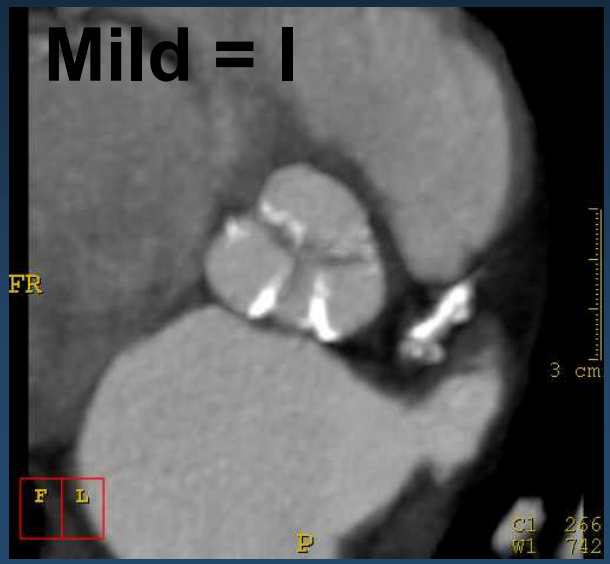
Precise screening due to

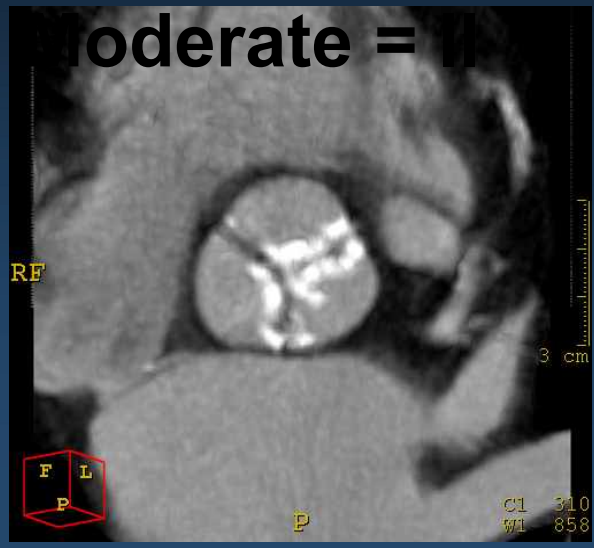
- limited amount of artifacts

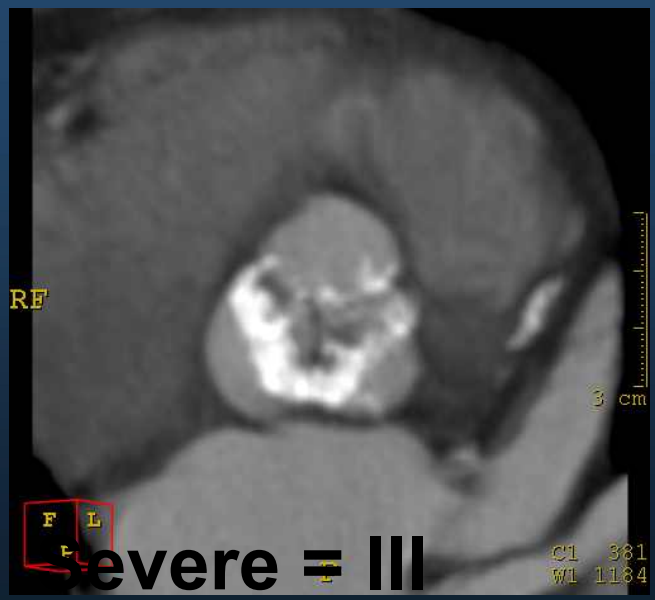
- ability for 3D reconstruction

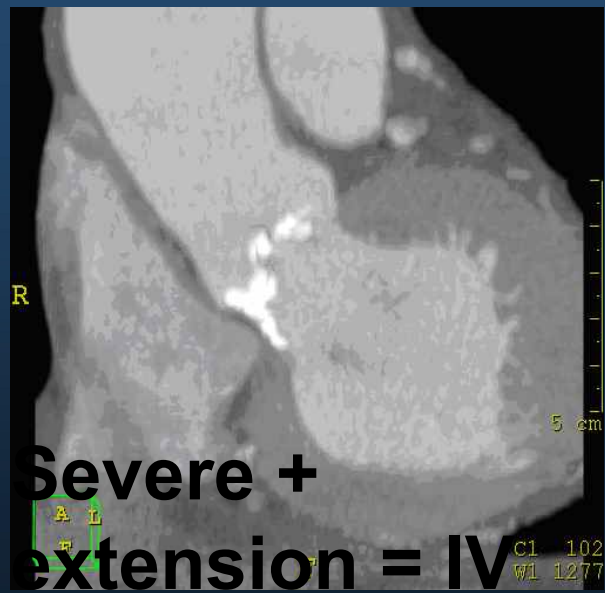
- good resolution

Annulus and LVOT Calcification Grades Correlate With AR - ‚Siegburg Score‘



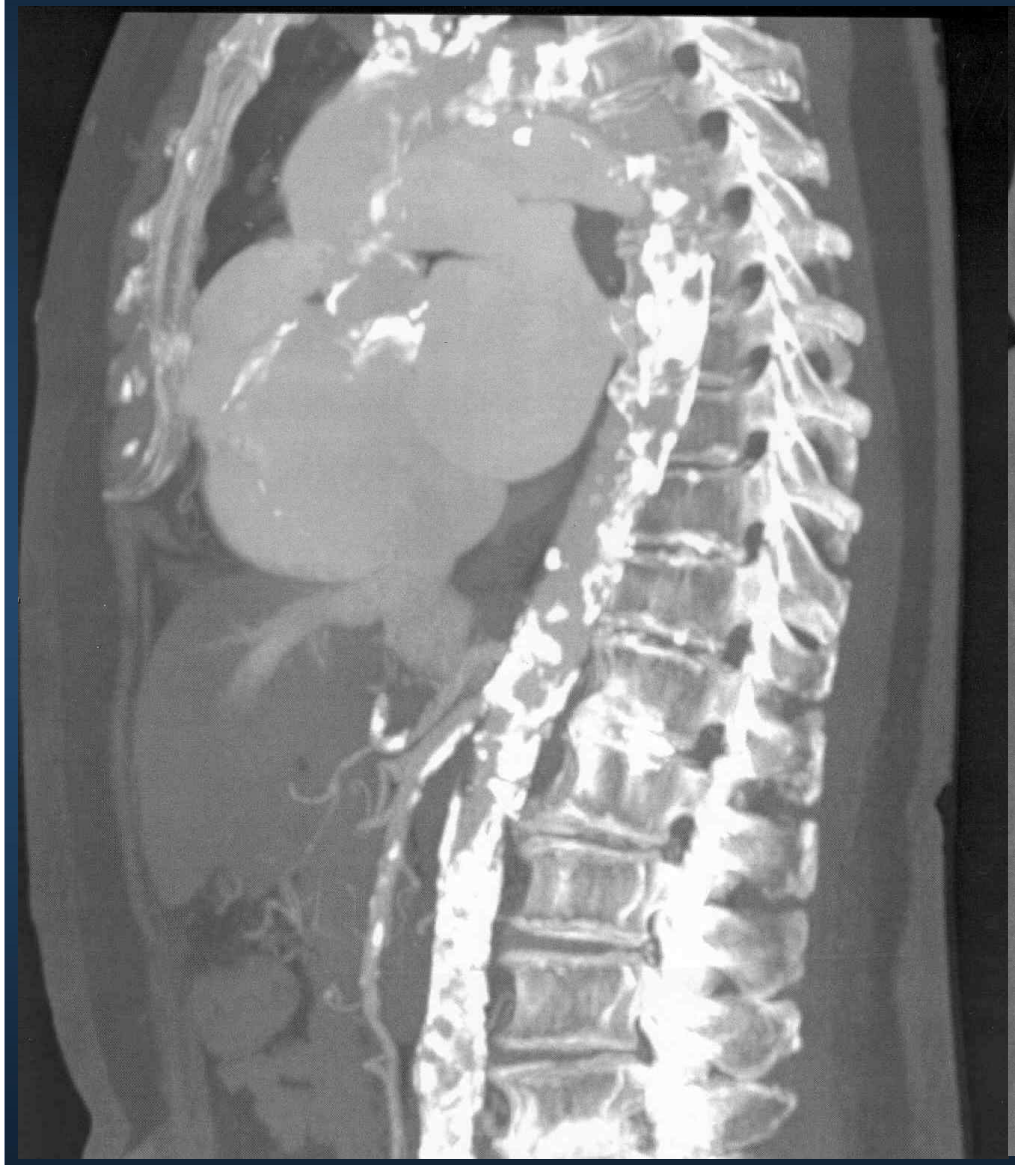


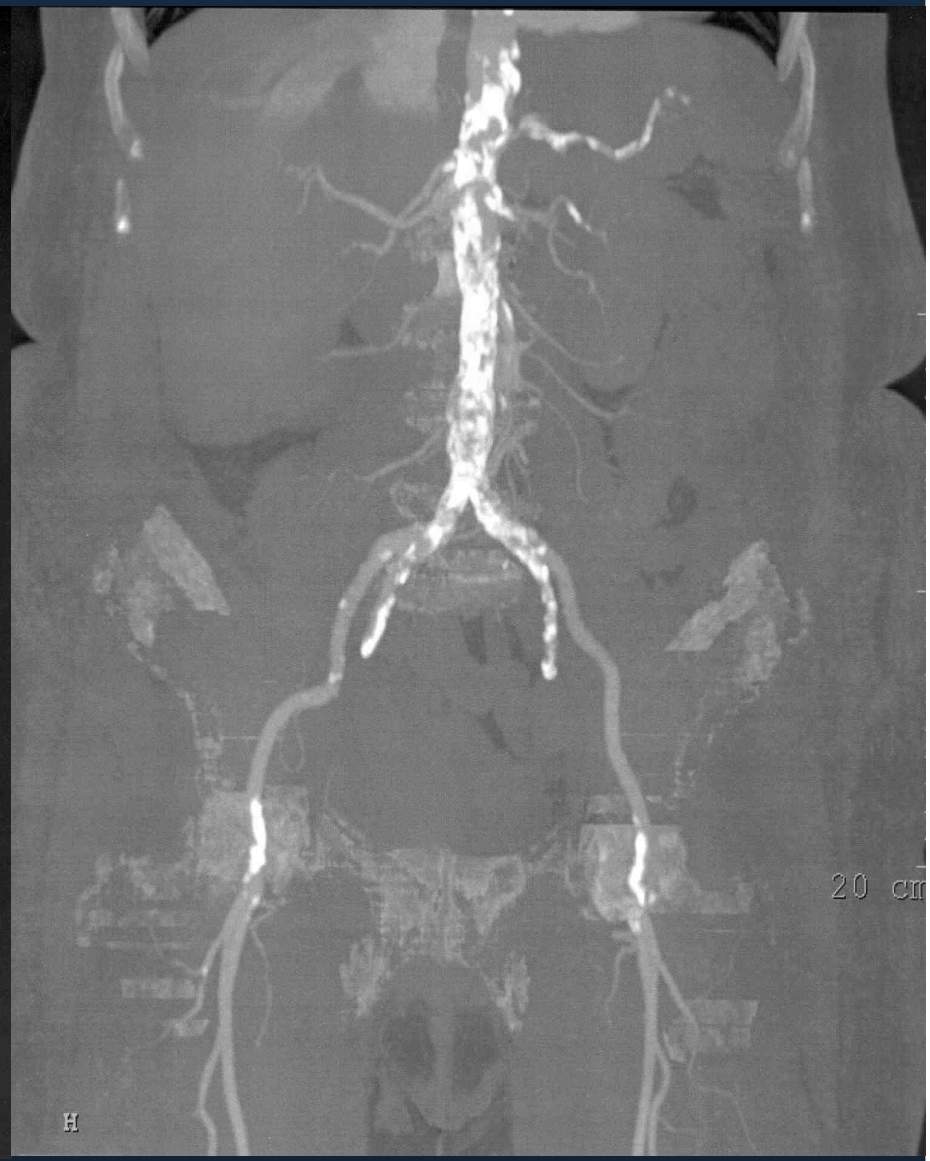




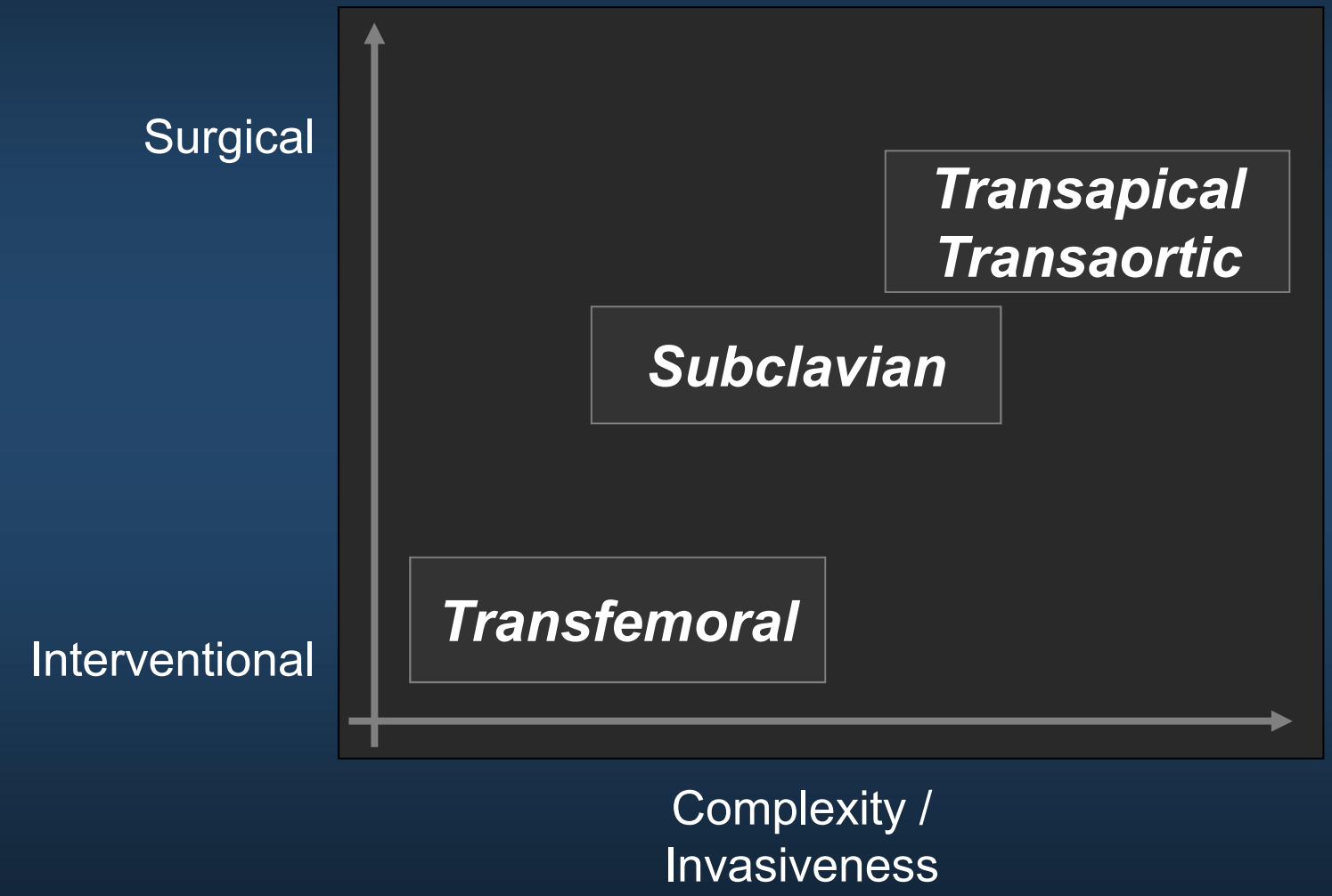
CoreValve – The Unsuitable Patient

Severe Calcifications of the Access

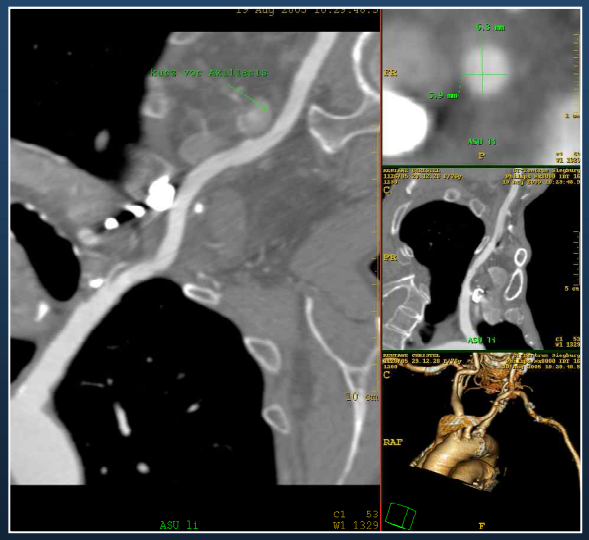


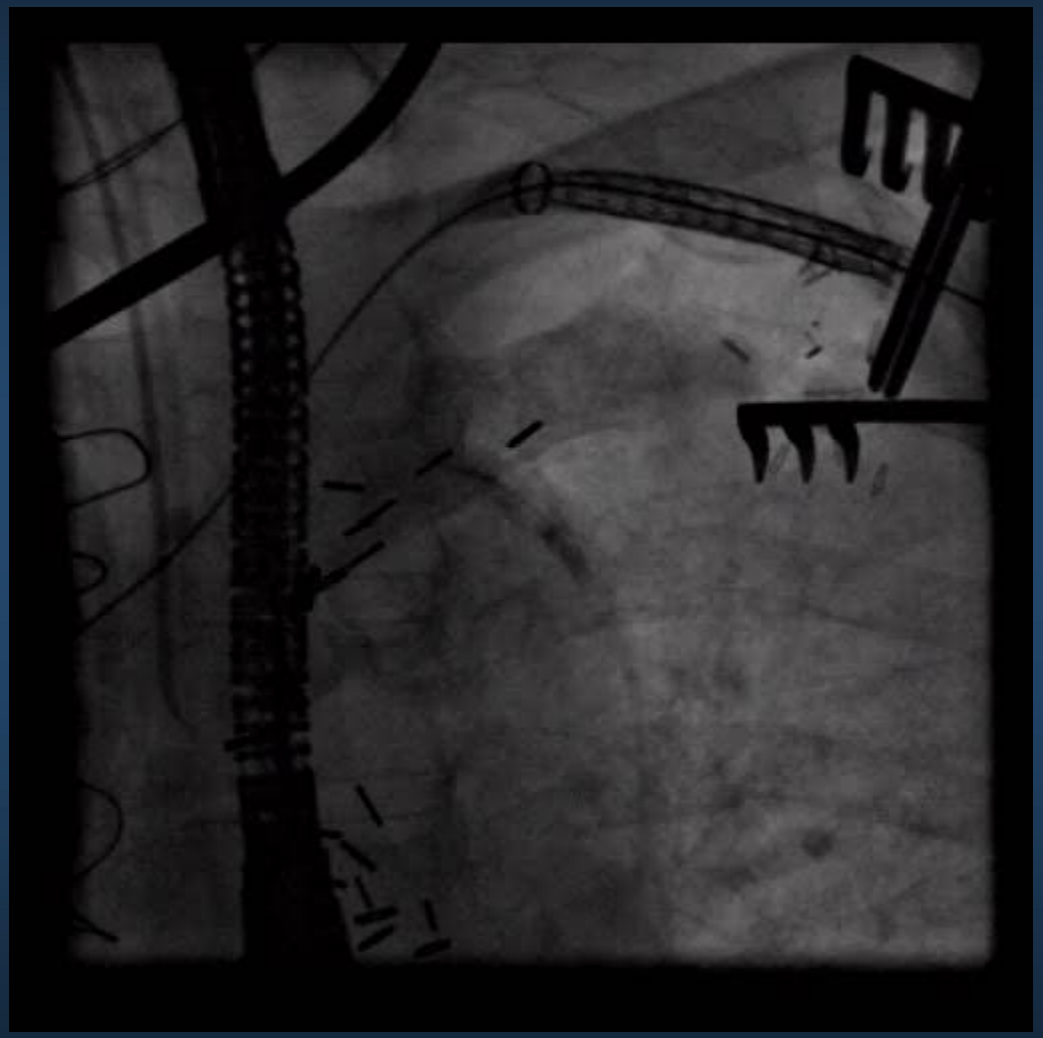


Which is the preferred access?

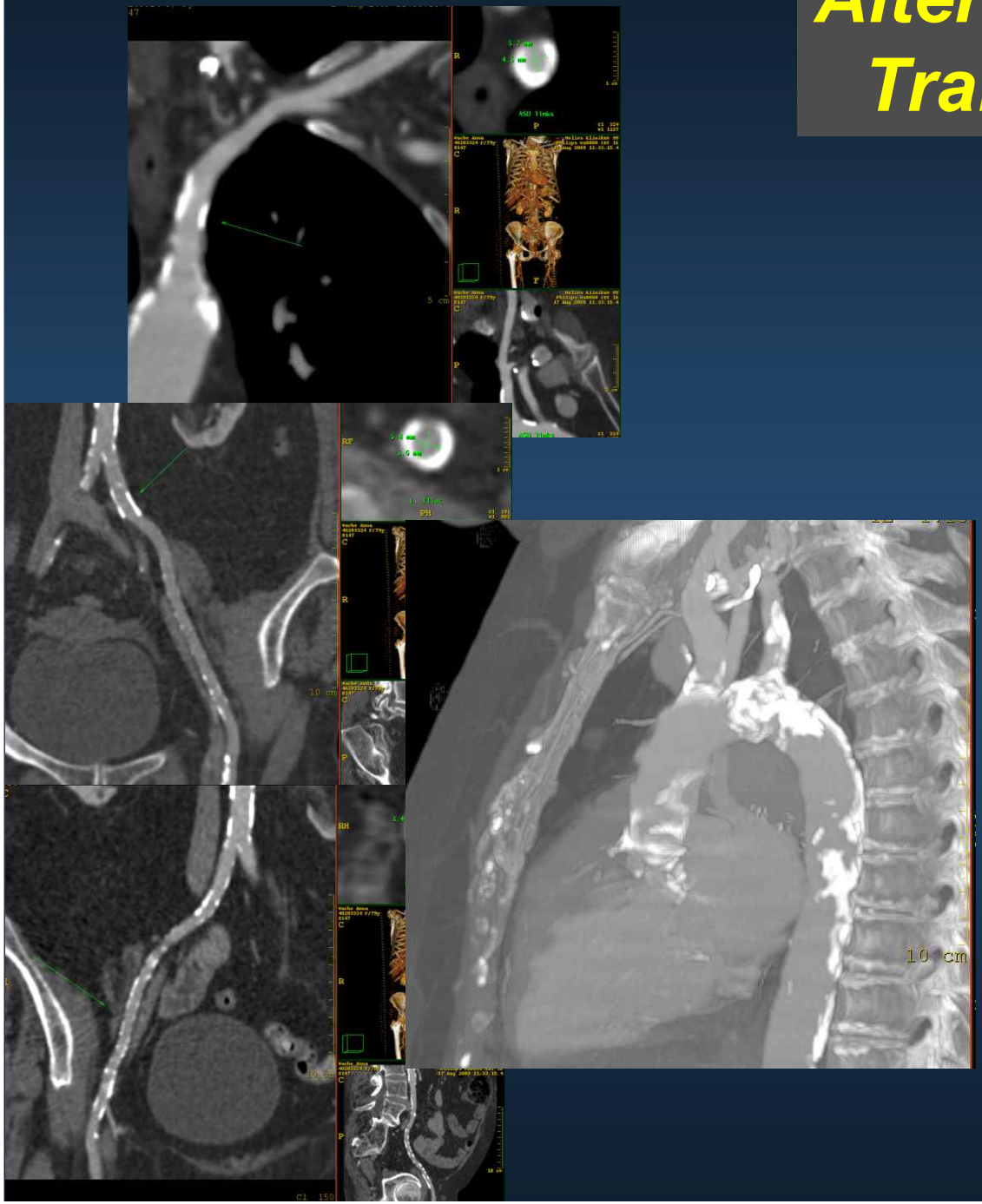


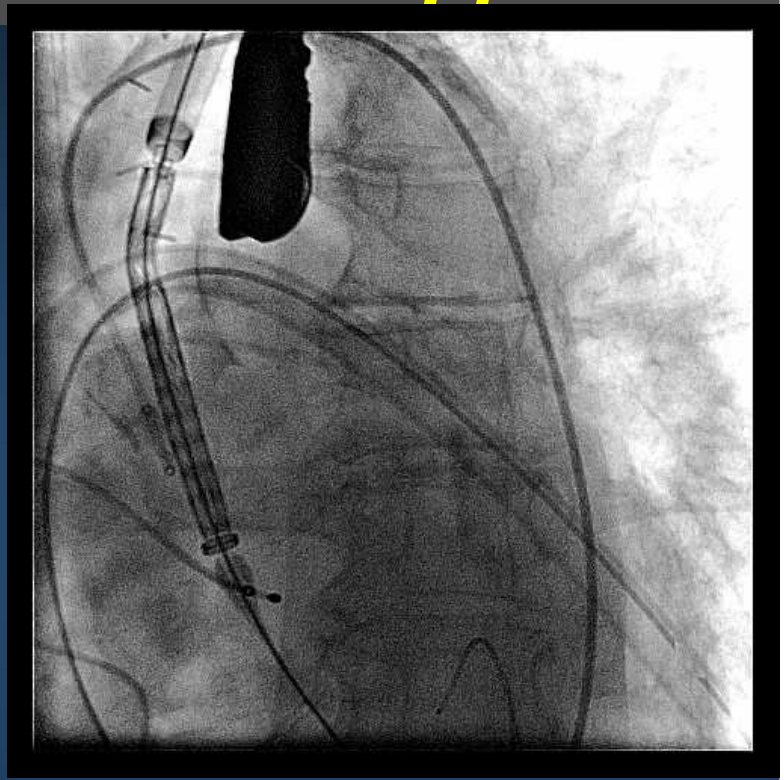
Subclavian Access

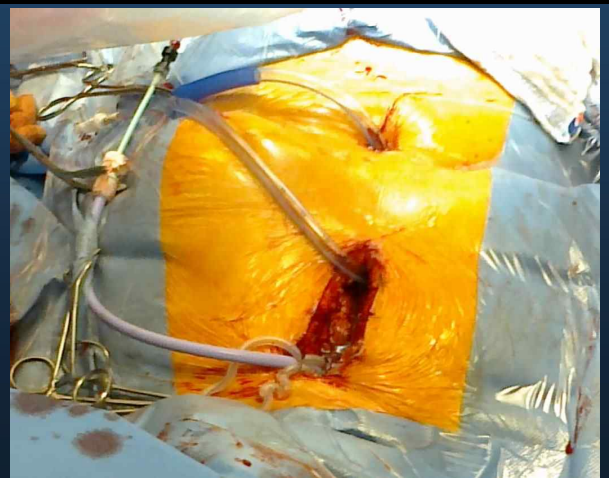




Alternative access sites
Trans-aortic Approach

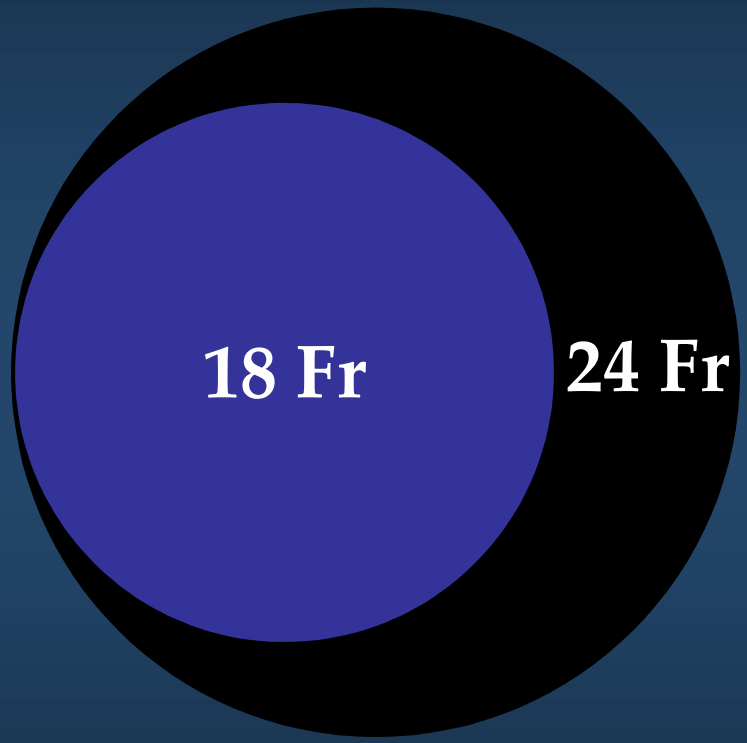






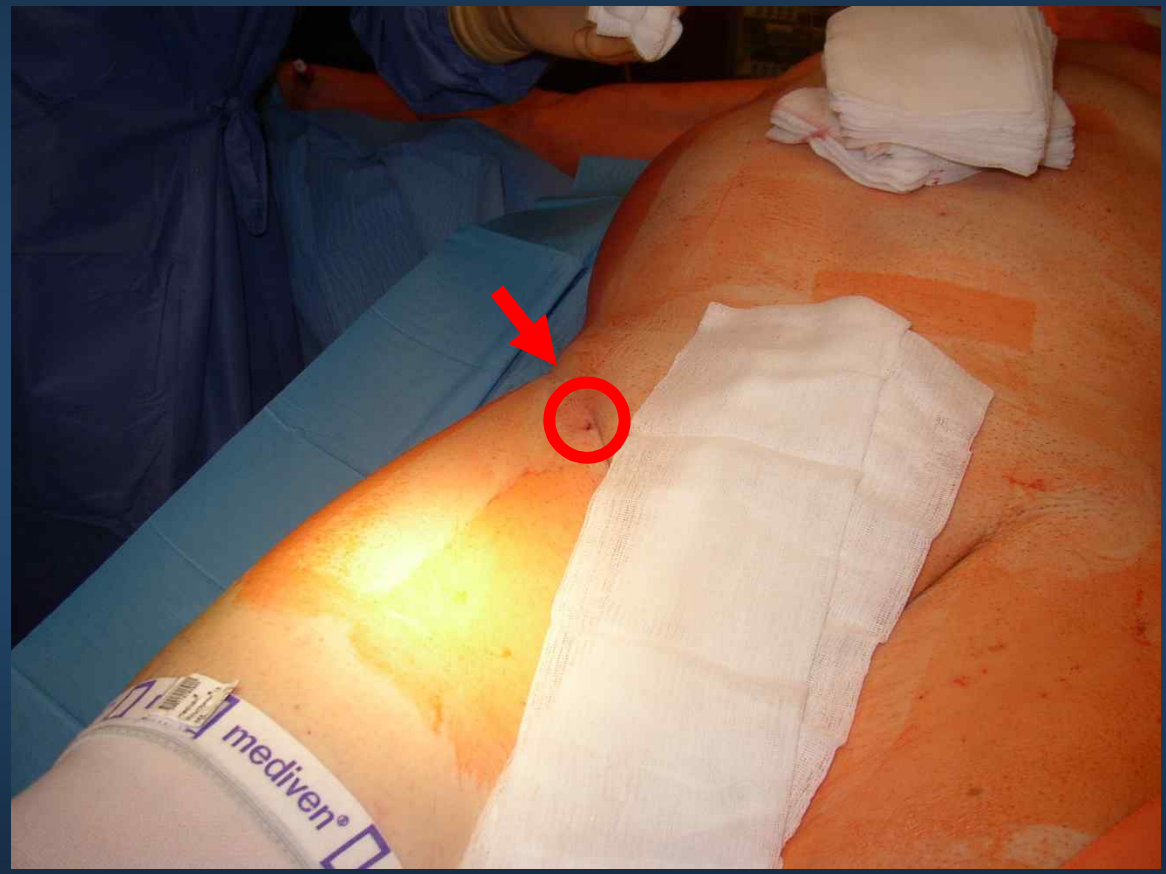
CoreValve Delivery Profile and Flexibility are critical

- Truly percutaneous delivery: minimizes risk of bleeding and vascular complications
- Easier delivery: for less experienced physicians
- Treating more patients: delivery is less hindered by peripheral artery disease
- Better options for additional approaches: such as subclavian and transaortic approaches



Drawn to scale

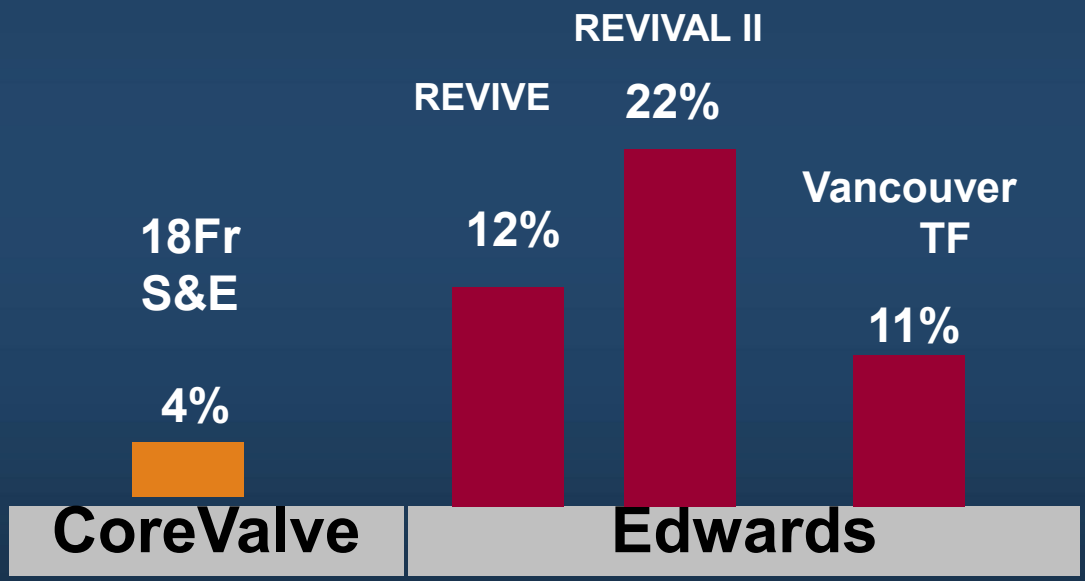
Low Profile !



Lower profile and flexibility means that CoreValve has a low rate of Vascular Complications

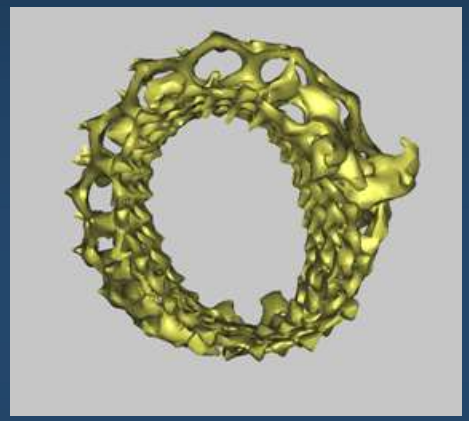
Vascular Complications

Patrick W. Serruys - PCR'08 Transcatheter aortic valve implantation: State of the art

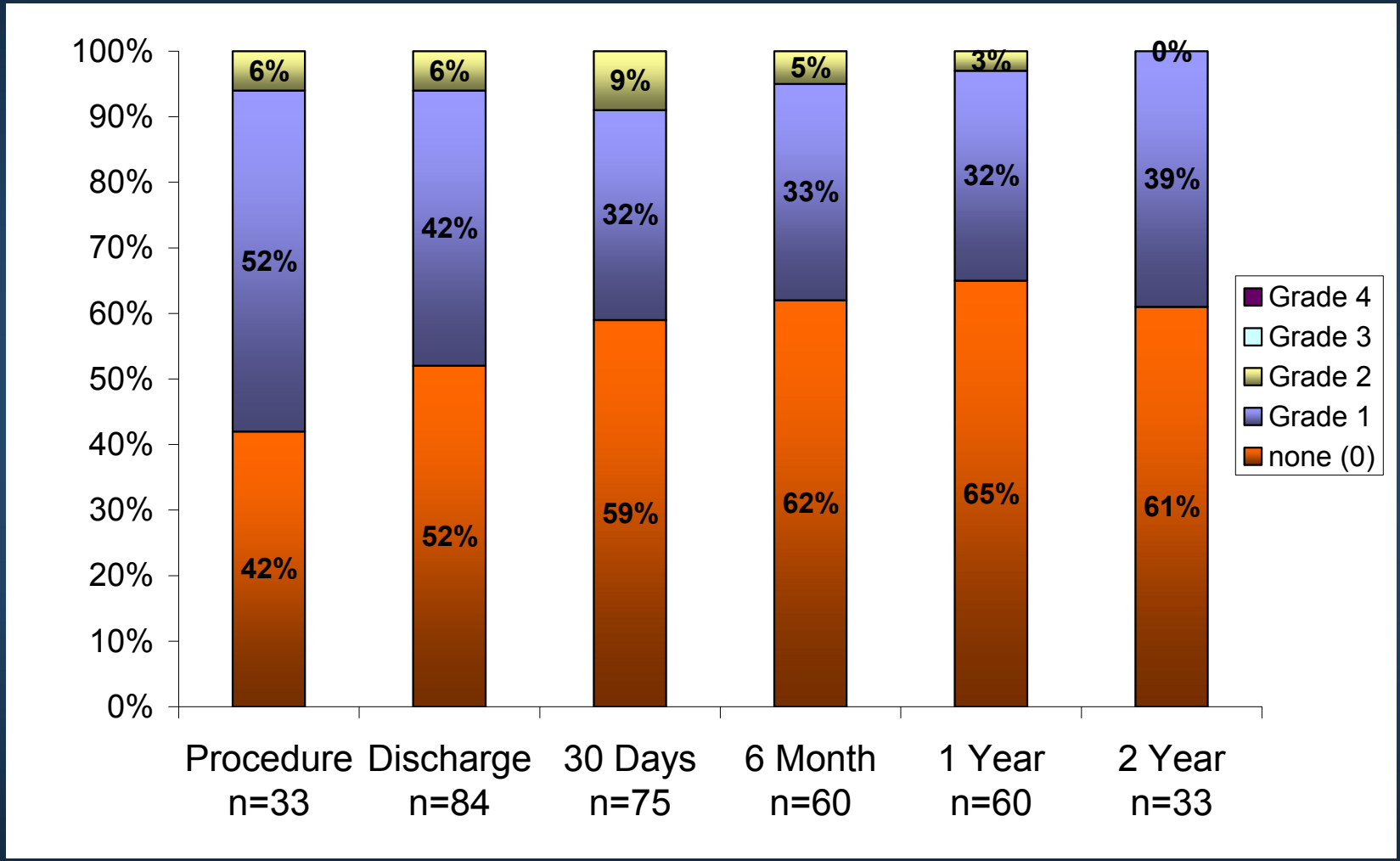


CoreValve is functioning well in Out-of-Round Situations

- **CoreValve has been shown to retain a round mid-section (where the leaflets are), even when the annulus was out of round**
  - "Dual source MSCT demonstrated incomplete and non-uniform expansion of the CRS frame, but the functionally important mid-segment was well expanded and almost symmetrical. Anatomical under sizing and incomplete apposition of struts was seen in the majority of patients." *(09/09) Schultz CJ, Weustink A, Piazza N, Otten A, Mollet N, Krestin G, van Geuns RJ, de Feyter P, Serruys PW, de Jaegere P. Geometry and degree of apposition of the CoreValve ReValving system with multislice computed tomography after implantation in patients with aortic stenosis. J Am Coll Cardiol 2009;54(10):911-918*



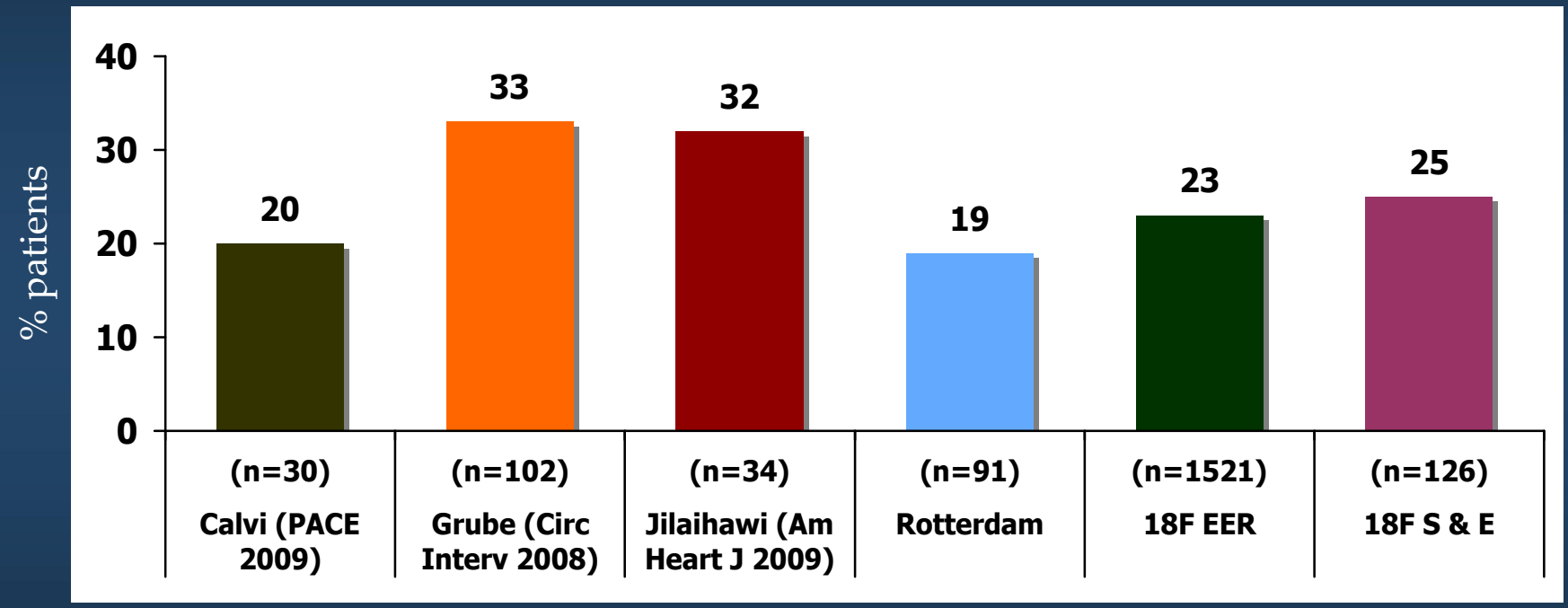
Aortic Regurgitation(PVL)



Source: 18Fr S&E

There Is a Higher Incidence of Pacemaker Implant Associated with CoreValve

New Permanent Pacemaker within 30 Days

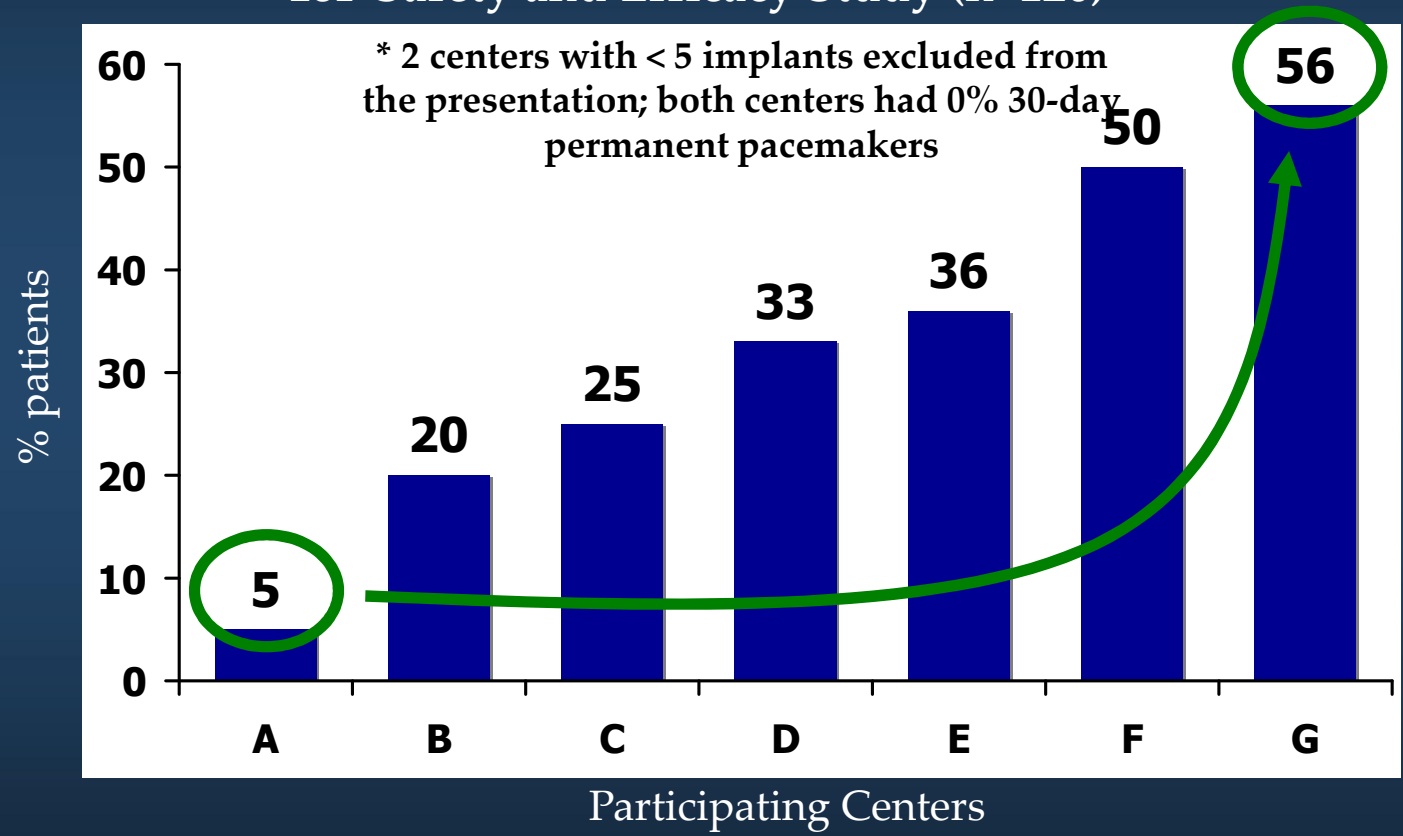


Weighted average = 23%
(n=1990 patients)

It is important to remember that pacemaker implantation may not mean pacing need

New Permanent Pacemaker within 30 Days

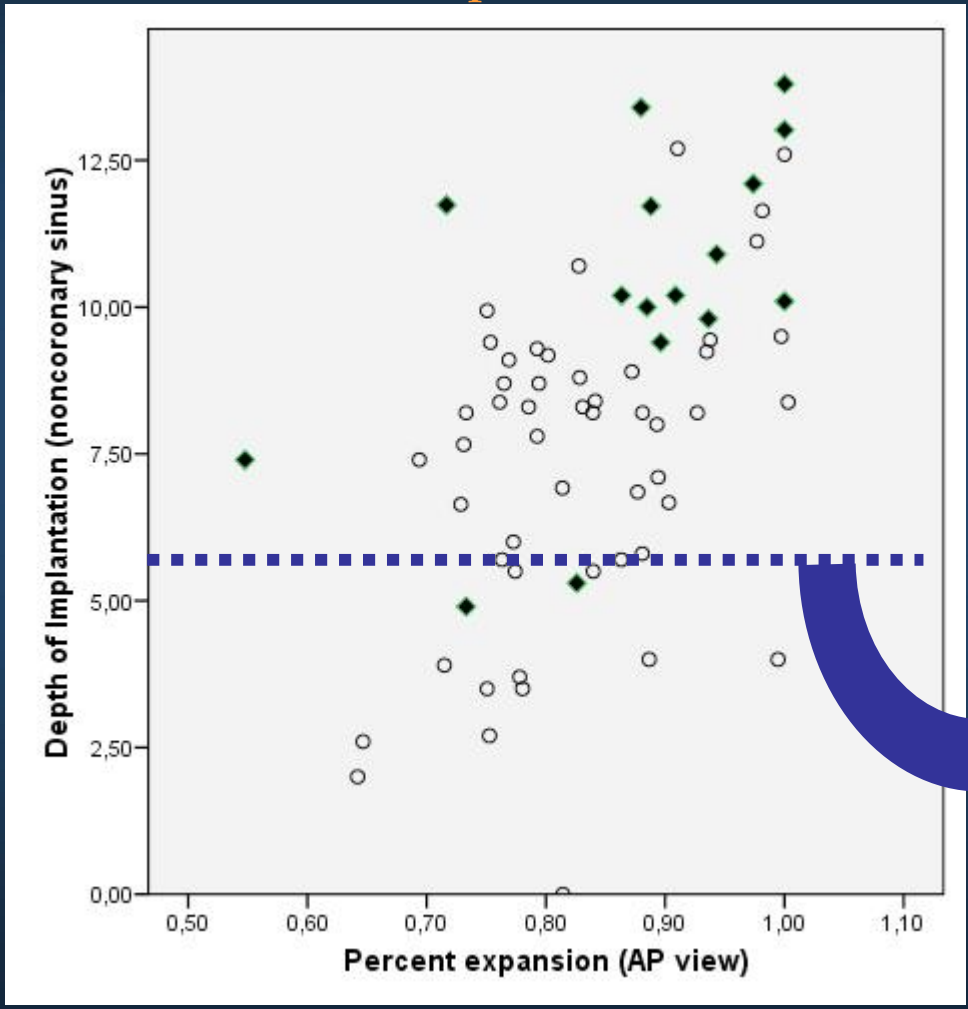
18F Safety and Efficacy Study (n=126)



Physicians' decision to prophylactically implant play a big role in the variability among centers

Depth of Implantation May Play a Role in the Onset of Rhythm Disturbances

Rotterdam Experience (n=91)



◆ New-onset LBBB acquired during or after valve implantation

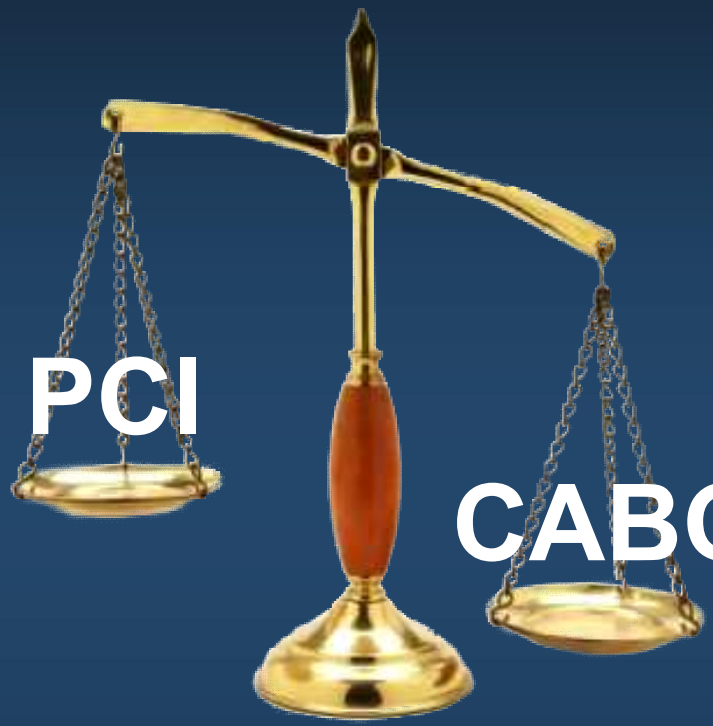
10.3 mm

○ No new-onset LBBB or new-onset LBBB acquired during procedure but before valve implantation

7.3 mm

6.0 mm

My Prediction: Repetition of an Old Story



1980's, 1990's

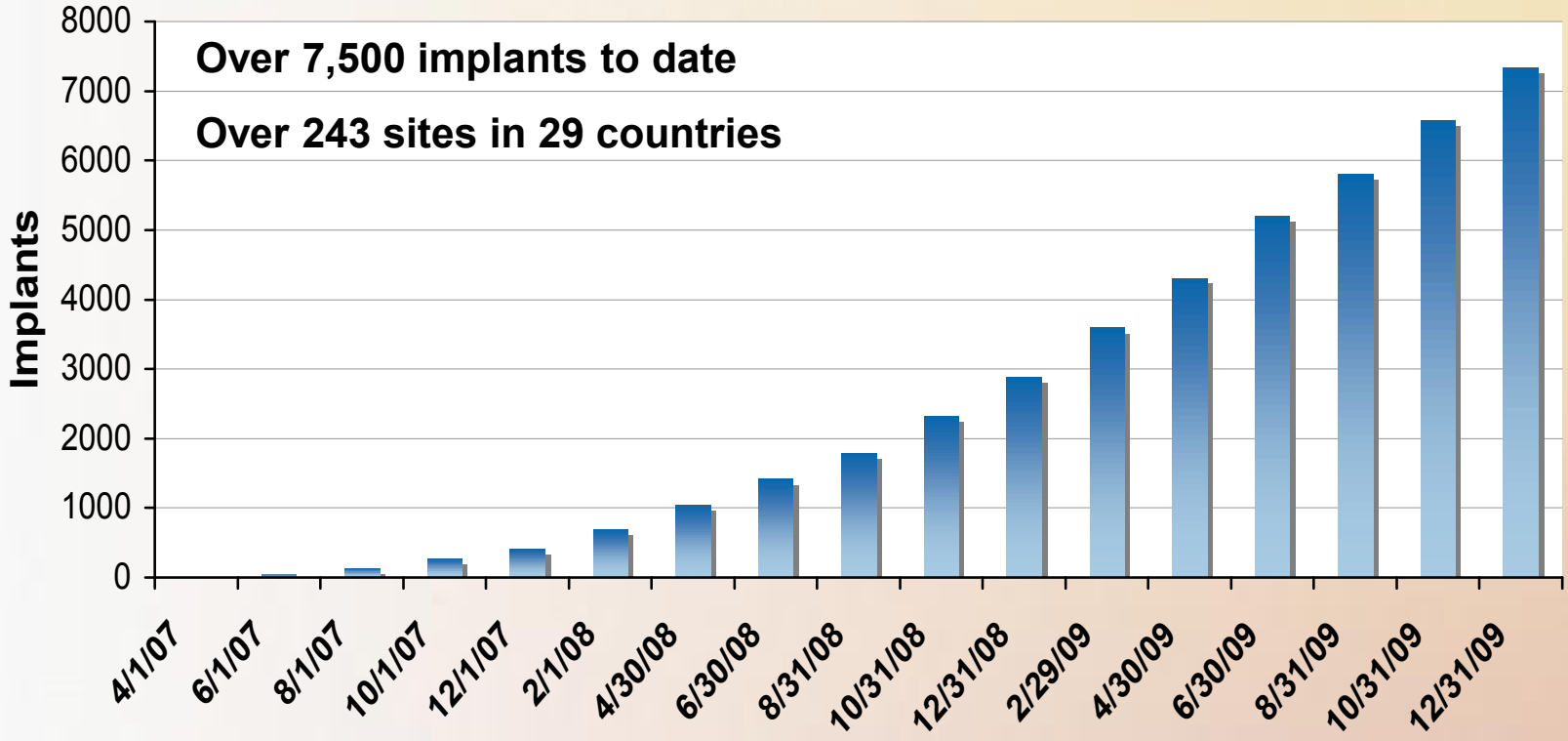
2000's, 2010's

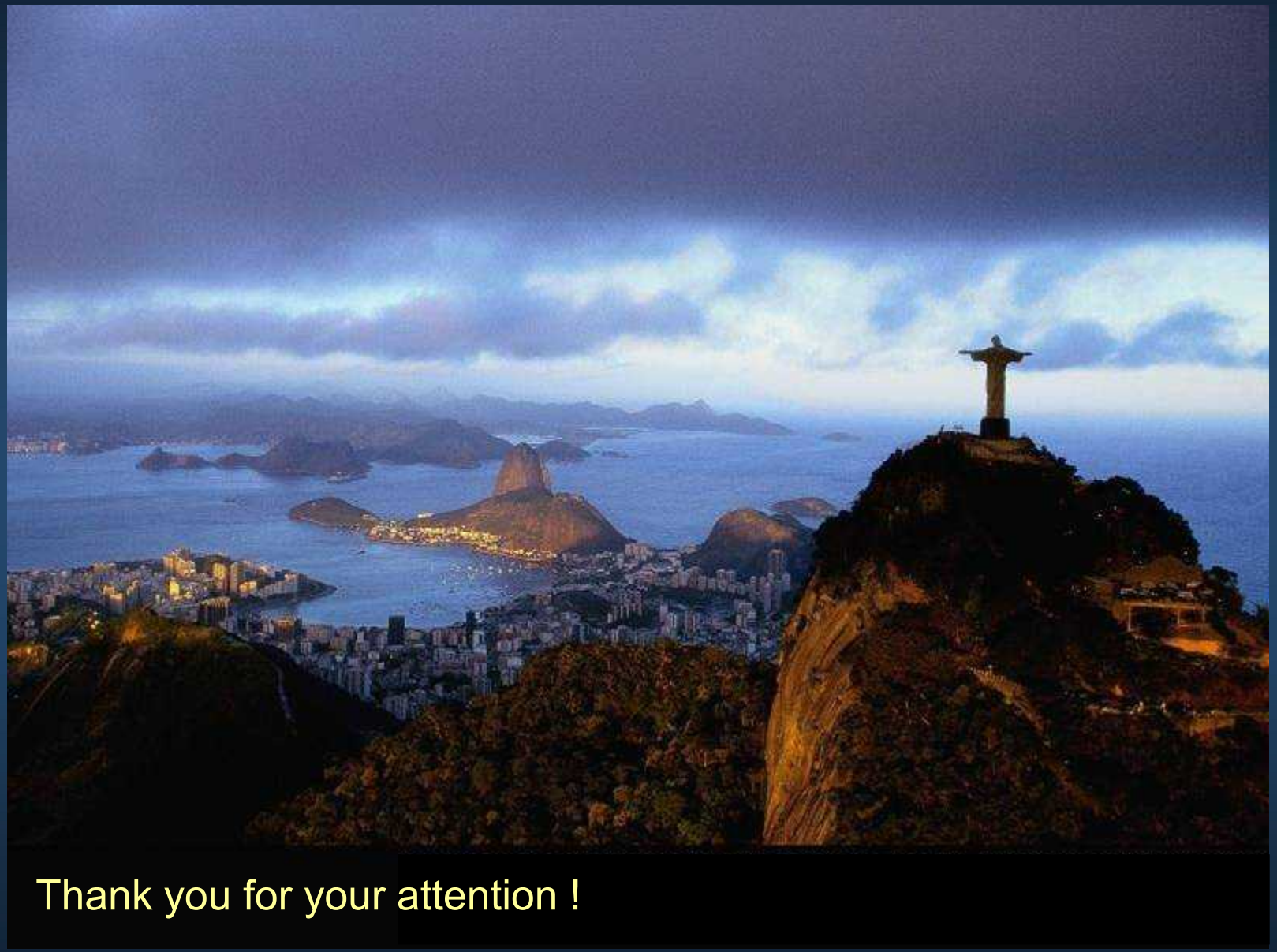
With the same result…

Thank you for your attention !

Questions ?

Clinical Experience to Date





Thank you for your attention !